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HEALTH TECHNOLOGY CASE STUDY 27:

Nuclear Magnetic Resonance Imaging Technology

A Clinical, Industrial, and Policy Analysis

SEPTEMBER 1984

This case study was performed as a part of OTA's Assessment of

Federal Policies and the Medical Devices Industry

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CONGRESS OF THE UNITED STATES
Office of Technology Assessment
Washington, D.C. 20510

J952-40

Recommended Citation:

Health Technology Case Study 27: Nuclear Magnetic Resonance Imaging Technology: A Clinical, Industrial, and Policy Analysis (Washington, DC: U.S. Congress, Office of Technology Assessment, OTA-HCS-27, September 1984). This case study was performed as part of OTA's assessment of *Federal Policies and the Medical Devices Industry*.

Library of Congress Catalog Card Number 84-601123

For sale by the Superintendent of Documents,
U.S. Government Printing Office, Washington, D.C. 20402

Preface

Nuclear Magnetic Resonance Imaging Technology: A Clinical, Industrial, and Policy Analysis is Case Study 27 in OTA's Health Technology Case Study Series. This case study has been prepared in connection with OTA's project on *Federal Policies and the Medical Devices Industry*, requested by the Senate Committee on Labor and Human Resources and endorsed by the Senate Committee on Veterans' Affairs. A listing of other case studies in the series is included at the end of this preface.

OTA case studies are designed to fulfill two functions. The primary purpose is to provide OTA with specific information that can be used in forming general conclusions regarding broader policy issues. The first 19 cases in the Health Technology Case Study Series, for example, were conducted in conjunction with OTA's overall project on *The Implications of Cost-Effectiveness Analysis of Medical Technology*. By examining the 19 cases as a group and looking for common problems or strengths in the techniques of cost-effectiveness or cost-benefit analysis, OTA was able to better analyze the potential contribution that those techniques might make to the management of medical technology and health care costs and quality.

The second function of the case studies is to provide useful information on the specific technologies covered. The design and the funding levels of most of the case studies are such that they should be read primarily in the context of the associated overall OTA projects. Nevertheless, in many instances, the case studies do represent extensive reviews of the literature on the efficacy, safety, and costs of the specific technologies and as such can stand on their own as a useful contribution to the field.

Case studies are prepared in some instances because they have been specifically requested by congressional committees and in others because they have been selected through an extensive review process involving OTA staff and consultations with the congressional staffs, advisory panel to the associated overall project, the Health Program Advisory Committee, and other experts in various fields. Selection criteria were developed to ensure that case studies provide the following:

- examples of types of technologies by function (preventive, diagnostic, therapeutic, and rehabilitative);
- examples of types of technologies by physical nature (drugs, devices, and procedures);
- examples of technologies in different stages of development and diffusion (new, emerging, and established);
- examples from different areas of medicine (e.g., general medical practice, pediatrics, radiology, and surgery);
- examples addressing medical problems that are important because of their high frequency or significant impacts (e.g., cost);
- examples of technologies with associated high costs either because of high volume (for low-cost technologies) or high individual costs;
- examples that could provide information material relating to the broader policy and methodological issues being examined in the particular overall project; and
- examples with sufficient scientific literature.

Case studies are either prepared by OTA staff, commissioned by OTA and performed under contract by experts (generally in academia), or written by OTA staff on the basis of contractors' papers.

OTA subjects each case study to an extensive review process. Initial drafts of cases are reviewed by OTA staff and by members of the advisory panel to the associated project. For commissioned cases, comments are provided to authors, along with OTA's suggestions for revisions. Subsequent drafts are sent by OTA to numerous experts for review and comment. Each case is seen by at least 30 reviewers, and sometimes by 80 or more outside reviewers. These individuals may be from relevant Government agencies, professional societies, consumer and public interest groups, medical practice and academic medicine. Academicians such as economists, sociologists, decision analysts, biologists, and so forth, as appropriate, also review the cases.

Although cases are not statements of official OTA position, the review process is designed to satisfy OTA's concern with each case study's scientific quality and objectivity. During the various stages of the review and revision process, therefore, OTA encourages, and to the extent possible requires, authors to present balanced information and recognize divergent points of view.

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[d] Background Paper #3 to *The Implications of Cost-Effectiveness Analysis of Medical Technology*.

[e] Background Paper #5 to *The Implications of Cost-Effectiveness Analysis of Medical Technology*.

[f] Background Paper #1 to OTA's May 1982 report *Technology and Handicapped People*.

[g] Background Paper #2 to *Technology and Handicapped People*.

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[1] Summer 1984.
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OTA Note

These case studies are authored works commissioned by OTA. Each author is responsible for the conclusions of specific case studies. These cases are not statements of official OTA position. OTA does not make recommendations or endorse particular technologies. During the various stages of review and revision, therefore, OTA encouraged the authors to present balanced information and to recognize divergent points of view.

1.
Introduction and Summary

1.
Introduction and Summary

INTRODUCTION

Nuclear magnetic resonance (NMR) imaging[1] is an exciting new diagnostic imaging modality that has captured the interest of the medical profession for a number of reasons. First, it employs radiowaves and magnetic fields rather than ionizing radiation, thus eliminating the risk of X-irradiation that is associated with use of devices such as X-ray computed tomography (CT) scanners. Second, in addition to providing excellent distinction between adjacent structures (spatial resolution), the technique uses differences in the density and the molecular environment of different substances to provide excellent tissue contrast without the need for injection of potentially toxic contrast agents. Third, because bone does not interfere with NMR signals (the absence of signal artifact from bone), physicians can visualize areas such as the posterior fossa, brain stem, and spinal cord with NMR that previously were not well seen with other noninvasive imaging techniques. Finally, and potentially of greatest importance, because NMR imagers are sensitive to fundamental physical and chemical characteristics of cells, the technique offers the *possibility* of detecting diseases at earlier stages than is currently possible and of permitting accurate diagnoses to be made noninvasively.

Along with these attractive attributes, however, NMR has its disadvantages. At present, NMR imagers are expensive, and installation of them is costly and logistically difficult. Furthermore, until (and possibly after) more experience with the modality is obtained, NMR imaging may require more *physician* time in performance of patient examinations than is the case with X-ray CT or other imaging techniques. Moreover, despite the rapid improvement in the quality of NMR images that has occurred over the past several years and the increasingly large number of clinical situations in which NMR imaging might prove to be of value, the exact role of NMR imaging in clinical medicine, particularly its efficacy compared to other imaging modalities, has yet to be defined.

Despite these concerns, NMR imagers are diffusing very rapidly. In January 1983, 14 units were in place in the United States outside manufacturers' facilities. By October 1983, 34 units had been installed in the United States, and by August 1984, at least 145 units were installed worldwide, of which 93 were in the United States.

Given the rapid rate of change in both the clinical and scientific status of NMR imaging, as well as in the number of units being installed worldwide, it is impossible to publish a review that accurately describes the "current status" of NMR imaging in almost any dimension. Such a review quickly becomes outdated as the field continues to evolve. This case study was written, therefore, with the following limited goals in mind:

- To provide a vehicle for gaining insight into the impact that Federal policies have had on the development of NMR imaging as a modality, on the industry that manufactures the imagers, on the hospitals and medical centers that might consider acquiring NMR imagers, and on a public interested not only in the timely introduction of valuable innovations, but also in protection from unsafe devices and rapid increases in health care costs. By identifying and analyzing a number of policy issues, the case study is intended to help the Federal Government and other interested parties assess the process through which new devices are made available.
- To make available a large amount of technical, clinical, industrial, and policy information under a single cover, and in the process to provide a "snapshot" view of the status of NMR imaging in several dimensions.[2]

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[1] The term "NMR imaging," used in this case study, is increasingly being replaced by the term "magnetic resonance imaging."

[2] The material was first compiled in fall 1983. App. C and policies of the Food and Drug Administration and third-party payers were updated in August 1984.

SUMMARY

The body of the case study is organized into nine chapters. Each of the chapters is briefly summarized below.

NMR—Historical and Technical Background

The existence of the NMR phenomenon was first demonstrated in 1946 by two American scientists, Felix Bloch and Edward Purcell, who jointly received the Nobel Prize for Physics in 1952 for their discovery. The first NMR image (of two tubes of water) was published by Paul Lauterbur of the State University of New York (SUNY) at Stony Brook in 1973, the same year X-ray CT scanning was introduced into the United States. Remarkable progress in the quality and capabilities of NMR imaging has been made in the years since Lauterbur imaged his two tubes of water, with no plateau in the rate of improvement in sight.

The nucleus of the hydrogen atom (proton)[3] has been most successfully exploited to produce high-quality NMR images because of its desirable magnetic properties and the high concentration with which it is present in the body. NMR images are fundamentally different from X-ray CT images. The latter rely on partial absorption and partial transmission of X-rays (linear attenuation) to produce images that reflect differences in the electron density and specific gravity of adjacent tissues. Proton NMR images are formed without the use of ionizing radiation and reflect the proton density of the tissues being imaged, as well as the velocity with which fluid is flowing through the structures being imaged and the rate at which tissue hydrogen atoms return to their equilibrium states after being excited by radiofrequency energy (proton relaxation time). The excitement about and investment in NMR have arisen from the belief that enormous clinical benefits might derive from the ability to obtain information about both the tissues of the body and certain kinds of chemical activity.

Clinical Applications of NMR

Concerns regarding the safety of NMR imaging have focused on magnetic fields and radiofrequency energy. To date, since adequate precautions have been taken, no significant biological risks associated with use of NMR have been identified. Other potential sources of concern relate to damage that could be caused by the possibility that metallic objects in the vicinity of NMR magnets could become projectiles, or that the strong magnetic fields used in NMR imaging could damage computer tape or other objects in the surrounding environment.

The National Radiological Protection Board in the United Kingdom is maintaining a record of patients and volunteers who have undergone NMR imaging studies in order to evaluate problems that arise in the future in individuals undergoing NMR scanning. The American College of Radiology is attempting to collect similar information in the United States. It would seem advisable to establish uniform guidelines for worldwide collection of this type of data, at least for the near future. Issues of who should be responsible for collecting and maintaining such data, and at whose expense, as well as issues pertaining to patient confidentiality, remain and need to be resolved.

The clinical application of NMR imaging in which the most experience has been gained and which so far has proven most efficacious is imaging of the brain and central nervous system. Results of studies of NMR imaging of the heart and pelvis are also particularly promising.

The scope of the role of NMR imaging in medicine is yet to be determined. Although there is some plausibility to the hundreds of applications that have been cited for NMR imaging, the majority of such applications must, for now, be considered potential rather than demonstrated.

Although future NMR production models are likely to simplify image acquisition for physicians, and although the time required to produce high-quality NMR images will likely decrease, it should not be assumed that images of the same quality as those being published by research institutions will necessarily be produced *immediately* in hospitals that are not able to spend equivalent time and effort on their production.

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[3] Since the hydrogen atom has one unpaired proton, the terms hydrogen atom and proton are used interchangeably.

In the early stages of evaluation of NMR imaging, many, if not most, of the patients that have been studied have appropriately been patients with known pathologies. It is not necessarily the case that NMR will be shown to have the same sensitivity and specificity when used to image patients with unknown pathology. Given the rapid improvements taking place in NMR imaging, however, current assessments may underestimate the ultimate sensitivity and specificity of NMR imaging in many applications.

It is likely that algorithms with pulse sequences (patterns of radiofrequency energy used to excite protons) specific to different pathologies will be built into NMR software in the future. While this means that NMR images of individual types of pathology are likely to become even better than they are today, it also means that if patients with unknown types of pathology are referred for a "screening" NMR scan, multiple scans, using multiple pulse sequences, may have to be performed in order to exclude with a reasonable degree of certainty the existence of an abnormality. Such use of multiple pulse sequences may increase the time and expense required to perform NMR studies.

To the extent that use of multiple pulse sequences does increase patient examination times, a tension may develop between the economic pressure to maintain reasonable patient flow and the clinical requirement that pathologic abnormalities be excluded with a high degree of certainty. To the extent that the latter predominates, the number of patients seen may decrease, producing a rise in average cost per NMR study. To the extent that the former predominates, the sensitivity and specificity of NMR may decrease.

Because the risks of NMR imaging appear to be low, NMR scans may be performed on patients repeatedly over time to monitor therapeutic progress or the natural history of disease. Such usage could result in increased demands being placed on NMR machines and in increased health care costs.

Within certain numerical ranges, relaxation times may provide sufficient pathologic specificity to be clinically useful. Because of overlap between the relaxation values of normal and abnormal tissues, however, relaxation times alone are unlikely to permit reliable pathologic diagnoses, despite the theoretical attractiveness of using such measurements. The possibility exists that nontoxic contrast agents can be devised that will enhance the pathologic specificity associated with relaxation time values. Considerable research remains to be done in the exploration of what physical, chemical, and biological factors give rise to and influence NMR relaxation times. Only through answers to these questions will it be possible to exploit relaxation times' full medical and scientific potential.

NMR is also used to perform in vivo phosphorus NMR spectroscopy, in which the "chemical shift" phenomenon is used to provide an indication of the relative concentrations in which compounds such as phosphocreatine, adenosine triphosphate, and inorganic phosphate are present in intact human tissues or organs. Much additional research is required before an assessment can be made of the extent to which in vivo NMR spectroscopy can be used to provide diagnostically useful information regarding the metabolic and functional status of normal and abnormal tissues.

It should also be recognized that the technology required for in vivo human NMR spectroscopy is considerably more sophisticated than that required to perform proton NMR imaging. Thus, most of the NMR imagers that are generally being installed in hospitals today cannot currently be used to perform NMR spectroscopy. Hospitals desirous of performing spectroscopy and imaging may need either to obtain more than one NMR machine or to tolerate potentially costly amounts of time while field strengths are changed and the NMR machine is not operational. For the present, in vivo NMR spectroscopy should be considered an exciting and promising area of research that is of questionable feasibility for most hospitals.

The NMR Imaging Device Industry

The NMR imaging device industry, as it now exists, is both dynamic and intensely competitive.

Since 1976, at least 23 companies worldwide have decided to enter the NMR imaging marketplace. Eight firms have reached an advanced stage of development, whereas at least three others are engaged in intermediate-level activities. The industry has a multinational character, with firms based in the United States, Japan, West Germany, Great Britain, France, Israel, and The Netherlands. All but three of the firms have multiple product lines. The industry appears concentrated among four firms, which accounted for 79 percent of the 145 known worldwide placements existing in August 1984.

At present, small firms can enter the market, but entry depends on several key factors, including their ability to attract capital and scientific or technical talent for research and development (R&D), to develop strong university or medical center ties for collaborative research, and to market products once they have been developed. The pathways to market entry are varied. but involve essentially four different routes: government-supported R&D, university-based R&D, acquired technology, and internally based R&D. Initial capitalization for market entry is estimated to be between $4 million and $15 million. University or medical center research ties are considered essential in the industry, and every firm that has attained either intermediate or advanced stage R&D has a close collaborative relationship with one or more universities or major medical centers.

The existence of at least 19 NMR imaging device manufacturers suggests that patents have not created a significant barrier to the entry of competitors into the marketplace. Whether patentable discoveries will emerge, prohibitively expensive cross-licensing agreements will be devised, or pending lawsuits will be settled in such a way as to change this situation is difficult to predict. It is also difficult to assess how beneficial the protection afforded by patents has been to the commercial development of NMR imaging in this country. It is possible, if not likely, that many manufacturers have opted to retain discoveries as "trade-secrets," rather than to reveal confidential information in patent applications.

There is considerable diversity in the product lines and operations of firms in the NMR imaging industry. Sixty-three percent of the companies manufacture non-health-care related products either directly or through a parent firm. Since the 1970s, the NMR imaging device industry has witnessed a large number of acquisitions, mergers, and trade agreements. At least three mergers in the industry have involved vertical integration either to acquire magnet manufacturing capabilities or to expand sales or distributorship networks to specific geographic areas. Vertical integration is expected to increase in the industry over the next 2 to 5 years.

Most firms in the industry believe that non-price factors will prove more important than product price in determining future NMR sales and market share. Product differentiation is expected to figure prominently in the non-price competition strategies of NMR imaging device firms. Manufacturers believe that the most important factors are likely to be image quality, product features or capabilities, product reliability, and product service. Various manufacturers are placing different emphasis on these factors as part of their marketing strategies. Buyers' perceptions of a corporation's chances for long-term survival will probably also be important.

It is expected that NMR imaging sales will become an important source of company revenues for many manufacturers over the next few years. Firms are expected to maintain heavy investment in R&D activities even after receiving Food and Drug Administration (FDA) premarket approval and introducing commercial NMR imaging prototypes. NMR sales could increase from $100 million per year in 1983 to $2.5 billion per year in 1988, amounting to an annual rate of growth in sales of 90 percent. The percentage of diagnostic imaging industry sales attributable to sales of NMR imaging systems could increase from 2.5 percent in 1983 to 30 percent by 1988.

Hospital Costs and Strategies

One of the major concerns that has emerged regarding NMR imaging relates to the impact this new technology will have on health care costs. These concerns derive in part from the high anticipated costs associated with the purchase and installation of an NMR imaging system and from uncertainties regarding the extent to which NMR imagers will be used in conjunction with other diagnostic modalities.

Capital and operating expenses for NMR imaging are primarily determined by the type of magnet (resistive, permanent, or superconducting) used to produce the static magnetic field. Purchase prices range from approximately $800,000 for a resistive system to $1.5 million for a permanent magnet system or a 0.5 tesla superconducting system and to over $2 million for a 1.5 tesla superconducting system. Installation costs range from $25,000 to $75,000 for a permanent magnet system to up to $1 million for a 1.5 tesla superconducting system. Estimates of the average cost of an imaging study, exclusive of professional fees, are difficult to make at this time, but range from as low as $180 for a resistive system to as high as $700 for a superconductive system. These estimates are quite sensitive to a number of key assumptions, such as the time needed to process patients.

The likely effect of NMR imaging on health care costs will depend on how it is employed by physicians in actual practice situations. Several factors need to be considered in this regard. First is the extent to which NMR imaging is performed instead of other diagnostic modalities in the management of specific patient complaints or disease entities. Second is the extent to which NMR is used in situations in which no diagnostic modality is currently used. Such situations are likely to include the use of sequential NMR scanning to monitor the natural history of diseases and the progress of chemo- and other therapies. Finally, much will depend on such factors as how much surgery is avoided, whether hospital lengths of stay are shortened, and whether diagnostic workups that were performed in the hospital are shifted to the outpatient setting.

Most of the early NMR units acquired by hospitals have been installed in university teaching hospitals. This situation is not surprising, given the interest such hospitals have in performing research and being at the "cutting edge" of medical developments, and given the research needs of manufacturers in order to obtain FDA premarket approval. In addition, university hospitals have been able to use their special strengths to obtain NMR imaging systems at decreased or nominal cost. Price and operating costs of experimental systems have frequently been further subsidized by research grants from manufacturers and have often been shared between hospitals and universities. These observations suggest that many of the university hospitals that have obtained NMR imaging systems to date may have done so in part because they did not have to be so concerned with acquisition costs and early operating costs as other hospitals have to be.

In 1983 the Veterans Administration (VA) decided to initiate a staged program of acquisition of NMR devices with a single NMR demonstration and evaluation project. The decision to acquire an NMR device for the VA system derived from an interest in "helping the VA march into the future" (171). No estimates of the impact of NMR on the cost of patient care were made. The decision to restrict the initial purchase to a single unit emanated from a concern about the rapid rate at which NMR technology was changing and the resultant desire to avoid installing a large number of systems that might soon become obsolete. NMR manufacturers have suggested, however, that due to the ability to upgrade their systems, early obsolescence may be less of a problem with NMR imagers than it was with X-ray CT.

Investor-owned hospitals have also followed a cautious approach to acquisition of NMR imaging equipment. The Hospital Corp. of America and Humana, for example, have each decided to acquire a small number of systems in the near future in order to conduct in-house evaluations of the cost, utility, and ideal configuration of NMR imaging systems in the community hospital setting. Others, such as American Medical International, National Medical Enterprises, and Lifemark, have postponed acquisition of NMR equipment until additional information regarding the cost, utility, and reimbursement rates for NMR imaging is available. Finally, investor-owned companies that operate hospital chains plan to use their ability to buy in volume to obtain special price consideration from manufacturers.

History of Funding for NMR Research

In the United States, both the National Institutes of Health (NIH) and the National Science

Foundation have provided considerable support to basic NMR research over the past decade. NIH is currently funding approximately $2 million in research in at least 10 different institutions relating to NMR imaging or in vivo spectroscopy. Announcement of awards from the Diagnostic Imaging Research Branch of the National Cancer Institute to assess the comparative efficacy of NMR imaging and other diagnostic modalities were made in mid-1984.

At least three different noncommercial entities provided support for NMR research in England and Scotland over the past decade. These include the Wolfson Foundation, and two government entities, the Medical Research Council and the Department of Health and Social Security in England.

Certain contrasts between the history of the development of NMR imaging in the United States and Great Britain can be identified. Unlike the situation in the United States, in Britain the government undertook a concerted effort to develop technology that might be of use specifically in hospitals. This effort was focused through a program funded by the Department of Health and Social Security which lent considerable financial support to the development of NMR imaging techniques. It is interesting to note, however, that once it became apparent that the development of NMR imaging systems was not only commercially viable, but also potentially extremely profitable, U.S. manufacturers rapidly and intensively began investing in NMR imager development programs.

In Britain there also seem to have been several interdisciplinary groups that collaborated on the development of NMR imaging techniques. In the United States, in contrast, most of the early work on NMR imaging was done by Lauterbur and Damadian with apparently little, if any, interaction between the two, despite the fact that both were at campuses of the State University of New York. There also seem to have been fewer centers in the United States in which scientists with varied backgrounds collaborated on the type of interdisciplinary research that resulted in the advances in NMR imaging that took place in Britain.

FDA Regulation

FDA authority over NMR imaging devices derives from two Federal acts: the Radiation Control for Health and Safety Act (RCHSA) of 1968 and the Food, Drug, and Cosmetic Act (FDCA), as amended in 1976. FDA has not established radiation emission performance standards for NMR devices under its RCHSA authority, and it is not likely that the RCHSA will have a significant impact on the development of NMR imaging as a medical diagnostic modality. The FDCA, in contrast, has had and continues to have a significant impact on the development of NMR imaging devices.

The 1976 Medical Device Amendments require that all medical devices be classified into one of three regulatory categories based on the extent of control necessary to provide reasonable assurance of safety and effectiveness. NMR imaging devices are the first imaging devices to be classified into Class III for which premarket approval (PMA) has been required. The premarket approval applications (PMAAs) submitted by three companies were deemed "approvable" by the FDA Radiologic Devices Advisory Panel in July 1983, and were granted formal premarket approval by FDA in spring 1984.

Some general insights into the PMA process can be gained from examining how NMR has fared in its interactions with it to date. It should be realized, however, that the experiences that an extremely promising, high R&D-cost device such as NMR has had with the FDA may not be representative of those that other devices may have in the future.

In the case of NMR, it appears that the FDA PMA process is primarily playing a quality-assurance role—a role that Congress intended it to play. PMA does not appear to have constrained NMR technological development. However, in its attempt to assist manufacturers and institutional review boards to define when experimental use of NMR does not pose a significant risk, FDA may have influenced the technological development of NMR devices.

FDA clearly has not constrained the number of NMR imagers that could be installed on an experimental basis in the United States. Of the approximately 34 NMR systems installed in the United States by October 1983, 15 were by a single manufacturer. It appears, therefore, that the FDA PMA process will not act as a major constraint on the rate at which NMR devices are adopted and used throughout the United States. This situation may, in large part, be a result of the long gestation period required for development of a production model of a high R&D-cost device, such as an NMR imager.

If PMA is not granted to other manufacturers in a timely fashion, however, manufacturers may begin to suffer from delays in receiving revenues to cover their development costs. Because the Health Care Financing Administration (HCFA) requires FDA approval of a device before it approves coverage for it, undue delay in PMA could injure manufacturers because of the constraining influence that the absence of Medicare reimbursement would have on hospital acquisition decisions.

Two final impacts of the FDA PMA process should be identified. First, in their quest for PMA, manufacturers have subsidized a considerable amount of research in order to establish the safety and effectiveness of NMR imaging devices. How much of this research would have been subsidized or performed by manufacturers in the absence of the PMA process is impossible to estimate. Finally, it appears that the PMA process may prove capable of conferring a competitive advantage upon those manufacturers who are first to receive PMA, particularly if third-party payers decide to approve coverage only for those manufacturers' devices that have received PMA. How much of a financial benefit, in both the short run and the long run, accrues to those "early bird" manufacturers who obtain PMA while others still await it may help determine not only the future of the NMR manufacturing industry, but also the speed with which manufacturers pursue development of other new technologies in the future.

Third-Party Payment Policies

In determining coverage policy for new medical technologies, third-party payers look first to FDA for some indication of a device's status. Third-party payers generally will not reimburse for clinical services performed with "investigational" devices. HCFA will provide coverage under the Medicare program only for those devices, services, or procedures that are determined to be both "reasonable and necessary." HCFA generally does not approve coverage of a new device unless FDA has already found it to be "safe and effective." FDA determination of safety and effectiveness, however, does not ensure that the device will satisfy HCFA's criteria of reasonableness and necessity.

Other third-party payers, such as State Medicaid programs, Blue Cross and Blue Shield plans, and private insurance companies consider similar factors in making coverage decisions, but vary in their general procedures, methods of assessment, and decision criteria.

HCFA conducts the most in-depth assessment of a new technology, with the aid of the Public Health Service's Office of Health Technology Assessment (OHTA).[4] In performing a technology assessment, OHTA gathers and analyzes relevant data on clinical safety and efficacy from various public and private sources. The assessment process often takes between 8 and 18 months to perform.

The national Blue Cross and Blue Shield Association also conducts technology assessments at the request of member plans. Association staff review available literature and elicit expert opinion from medical specialty societies in determining the safety and effectiveness of a new device. Staff assessments of new technologies frequently result in Uniform Medical Policy statements, which are intended only to guide coverage policy decisions of member plans. Each plan, however, may make its own independent coverage decision.

Commercial insurance companies follow a less formal procedure in conducting technology assessments. The Health Insurance Association of America (HIAA), a private organization serving the commercial insurance industry, furnishes information on new technologies to its members. At the request of a member company, HIAA will solicit an expert opinion regarding a new device from the Council on Medical Specialty Societies. The information will be synthesized and forwarded to member companies, who independently interpret it and make coverage policy decisions.

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[4] This executive office differs from the Health Program in the Congressional Office of Technology Assessment.

The major third-party payers also differ in the criteria they employ in setting payment levels for covered services. Important factors in these decisions include where the technology will be used (e.g., hospital, physician's office), in what circumstances it will be used (e.g., certain clinical situations or diseases), and by whom it will be used (e.g., physicians with general versus specialty training). Payment levels are generally based on criteria of "prevailing, customary, and reasonable" charges, allowing for differences in geographic area, past experience of individual practitioners, and prevailing market prices or fees.

Third-party payers are evaluating their coverage of NMR imaging. Some third-party payers have already begun to pay for NMR scans. Technology assessments of NMR imaging are now being performed by OHTA (for the Medicare program) and by the Blue Cross and Blue Shield Association.

State Certificate-of-Need Programs

Although State certificate-of-need (CON) programs were never specifically intended to constrain the diffusion of medical technology, they constitute one of the major policy mechanisms available to health planners for control over technology adoption. CON review of "need" may be based on numerous factors, including clinical use of technology, institutional characteristics, economic and financial effects, and population-based considerations. In the past, CON programs have employed at least four different policy orientations or strategies regarding technology introduction and distribution: pro forma denial, formalized strategy of delay, predetermined limits on diffusion, and uncontested approval.

The CON experience with X-ray CT scanners points out two problems that could arise in the future with NMR imaging: the fragility of shared-service arrangements among hospitals and the creation of incentives that encourage "anticipatory acquisition" of new technology. The latter situation can produce a "franchising" effect whereby hospitals that adopt technology early—often while the technology is still considered "investigational"—become well-positioned to keep the technology once its status changes and diffusion accelerates. Those hospitals that wait to submit CON applications risk being "disenfranchised" from obtaining the technology.

Various State and local planning agencies report increasing CON activity related to NMR imaging. As of September 12, 1983, at least 33 CON applications for NMR had been reviewed nationwide. Of these, 19 had received approval: 16 by State Health Planning and Development Agencies and 3 by local Health Systems Agencies. Twenty-five health planning agencies across the Nation also reported that they either had NMR-specific review criteria in force or were planning to develop them in the near future. Pending or recently enacted State legislation or regulations related to NMR were reported in at least six States.

Several distinct CON strategies regarding NMR appear to have emerged among the States. For example, New York, Illinois, Ohio, New Jersey, and Kentucky have each adopted predetermined limits on NMR imager diffusion. The Southeast Kansas Health Systems Agency has invoked a moratorium on NMR until community hospital planning has been completed. The District of Columbia CON program also has statutory power to employ a formalized strategy of delay. Nebraska, by contrast, is encouraging group applications involving shared-service arrangements among hospitals. Utah and California, through recent amendments to their respective State CON laws, appear to be following a strategy of uncontested approval for NMR imagers. No CON program, on the other hand, has adopted a policy of pro forma denial. It is anticipated that CON agencies will witness a rapid increase in the number of NMR applications filed by hospitals once HCFA policies regarding NMR are finalized.

Regulatory Overview

Since FDA has granted premarket approval to the first NMR imaging manufacturers, third-party payers have a position of major influence over the rate at which NMR imagers are acquired by hospitals. This influence will derive from their decisions regarding: 1) whether to cover use of

NMR imaging at all; 2) whether to cover NMR devices only of those manufacturers that have received premarket approval or those of any manufacturer; 3) which types of NMR scans to cover (e.g., head studies only or head and body studies); 4) the monetary level at which use of NMR will be reimbursed; and 5) the level at which professional fees for NMR imaging are set. If initial coverage of NMR is limited to a small number of clinical circumstances or reimbursement rates do not reflect the increased professional time that will initially be required for NMR scanning, hospitals may be restrained in the speed with which they acquire NMR devices.

The introduction of prospective payment based on diagnosis related groups (DRGs) under Medicare is also expected to affect the rate of diffusion of NMR devices into hospital settings. Hospitals now have to weigh financial considerations against patient care benefits more carefully when deciding whether to acquire an NMR imager and in deciding how an acquired NMR scanner is to be used. For some hospitals, such as municipal facilities serving large Medicare and Medicaid populations, the DRG payment system may exacerbate an already financially distressed situation and further impede those institutions' efforts regarding capital formation. The net effect may be to weaken the hospitals that serve as primary sources of care for disadvantaged populations. The ultimate impact of the prospective payment system on acquisition of NMR scanners is likely to depend on future HCFA decisions regarding recalibration of DRG payment rates to take account of introduction of new technology over time and regarding inclusion of capital expenditures in the DRG rate.

The final major regulatory influence on the rate at which new technology, such as NMR imagers, diffuses throughout the medical system is State certificate-of-need (CON) policies. There is already evidence that CON agencies are delaying the acquisition of NMR devices by some hospitals. Whether State agencies are adequately informed to be able to make appropriate decisions regarding whether and when NMR scanners should be introduced into hospitals is questionable.

A number of problems with CON policies that have appeared over the past decade in the experience with X-ray CT are likely to affect the course of NMR as well. Evidence for "franchising" and "anticipatory acquisition" of NMR is already available and will need to be addressed by CON programs. In addition, there is evidence of considerable interest on the part of private radiology groups, as well as hospitals, in establishing outpatient diagnostic centers which will include, but not be limited to, NMR devices. In most States, such ambulatory placements do not require CON approval. If State agencies are interested in controlling the introduction of new technologies, such as NMR, they will have to address themselves to this limitation in their purview. Alternatively, CON agencies could leave control over the "introduction" of technology to the FDA and third-party payers and concentrate on playing a complimentary role by assuring equitable distribution of new technologies within their jurisdictions.

In addition to these influences on the *rate* at which new technologies such as NMR imagers diffuse, two final policy issues should be addressed. First, there appears to be a large amount of duplicated effort on the part of FDA, third-party payers, CON agencies, and hospitals with regard to the assessment of new technology. Although it is unclear whether it would be beneficial to increase the coordination among these separate technology assessment efforts, the issue should be addressed. If HCFA is to continue relying on the Public Health Service's OHTA as an impartial source of advice, attention should be given to whether the resources available to OHTA are adequate.

Finally, as more technologies become available, it becomes increasingly important that the comparative efficacy of each be adequately evaluated and defined. How such comparative efficacy data will be acquired and who will fund the studies necessary to generate them are increasingly important issues that the Federal Government and others need to address if appropriate reimbursement policy decisions are to be made. In the case of a rapidly evolving technology, such as NMR imaging, the question of when to perform such comparative assessments also needs to be addressed. This "moving target" issue has hampered comparative efficacy assessments in the past.

2.

NMR—Historical and Technical Background

2.

NMR— Historical and Technical Background

It is not possible to provide either a comprehensive historical profile of nuclear magnetic resonance (NMR) or a detailed technical explanation of the NMR phenomenon within the scope of this document. In order to fully appreciate the excitement about the implications of being able to produce hydrogen or other atomic images using NMR, however, it is essential that the reader have some historical and technical background. The following sections attempt to provide that background. The first section discusses the historical development of NMR. The second section provides basic technical background about NMR and NMR imaging, including a description of the technical components used in NMR imaging systems. The final section introduces the types of magnets used in NMR imaging. Appendix A contains additional technical information.

HISTORICAL BACKGROUND

The existence of the phenomenon of nuclear magnetic resonance was predicted by a Dutch physicist, Gorter, in 1936. Gorter sought, unsuccessfully, to demonstrate the NMR phenomenon in lithium fluoride. A decade later, in 1946, two American scientists, Felix Bloch and Edward Purcell, working independently, simultaneously discovered and demonstrated the existence of NMR. Bloch's observations were made with studies of water at Stanford; Purcell's with studies of paraffin wax at Harvard. The two were jointly awarded the Nobel Prize for Physics in 1952. Since then chemists and physicists worldwide have routinely employed uniform magnetic fields in what can now be considered "conventional NMR spectroscopy" to study the molecular structure and dynamics of small homogeneous specimens (8). The NMR imaging techniques that have evolved over the past decade derive in large part from the 25 years of experience that had been accumulated prior to 1973 in the application of NMR spectroscopic techniques to the study of solids and liquids.

The establishment of a magnetic field gradient (a magnetic field that increases or decreases in strength in a given direction along a sample) across a sample was the key to going from spectroscopy to spatially encoding the information that forms the basis of NMR tomographic imaging. Although magnetic field gradients had been employed by scientists since the 1950s in studies of molecular diffusion in liquids (78), phase separation (separation of homogeneous but physically distinct portions of matter) in helium solutions (199), and methods of information storage (7), it was not until 1971 that Paul Lauterbur working at the State University of New York (SUNY) at Stony Brook conceived of the idea of manipulating magnetic field gradients to obtain a two-dimensional NMR image (116).[1] In his now classic experiment in which the first NMR image was produced, Lauterbur rotated magnetic field gradients (changed magnetic field gradients) in a technique he called zeugmatography to reconstruct a two-dimensional image of two tubes of water (115) (see fig. 1). In discussing the implications of his results, Lauterbur recognized the potential applicability of his technique to the imaging of soft tissue structures and malignant growths in vivo (115).[2]

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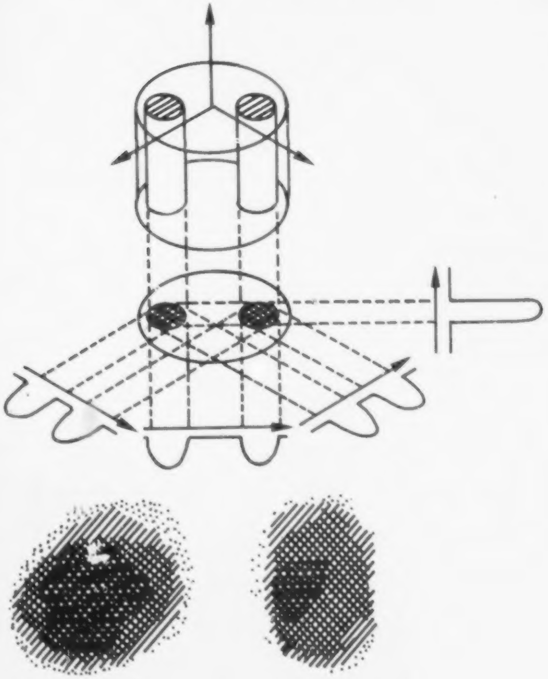
[1] Lauterbur was aware of the studies performed by Damadian (42) and Hollis (93), which demonstrated that excised tumors manifested prolonged NMR relaxation times. Recognizing that it might be tremendously beneficial to be able to make such measurements in vivo, Lauterbur worked to develop a technique in which NMR could be used to produce images (116).

[2] In 1973, Mansfield and Grannell published a letter in which they described a method, involving magnetic field gradients, through which NMR could be used to determine spatial structure in solids (121). No mention is made in the letter, however, of a proposal to use NMR to produce images.

Figure 1.—First NMR Image



NMR image of two tubes of water

SOURCE: P. C. Lauterbur, "Image Formation by Induced Local Interactions: Examples Employing Nuclear Magnetic Resonance," *Nature* 242 (5394): 190-191, Mar. 16, 1973.

Remarkable progress in the quality and capabilities of NMR imaging has been made in the 10 years since Lauterbur imaged his two tubes of water. In 1974, Peter Mansfield and his colleagues at Nottingham University published the first crude NMR medical image (of a human finger) (122). Only the gross outline of the finger without any internal detail was revealed. Improved images of human fingers were produced by the same group 2 years later using a different imaging technique that relied on selective radiation[3] of the specimen in switched magnetic field gradients (123). In 1976, Damadian and colleagues, working at SUNY at Brooklyn, employed a Field Focussing Nuclear Magnetic Resonance technique (FONAR) to produce the first NMR image of a tumor in a live animal (44). A year later a human wrist was imaged (91) and the first in vivo human whole-body NMR tomographic scan (image of an individual slice) was produced (43). In the latter scan, crude by current standards, the heart, lungs, mediastinum, and descending aorta could be detected (43) (see fig. 2). In 1978 a team led by Hugh Clow and Ian Young, working at English Music Industries' (EMI's) laboratories in London, produced what is believed to be the first NMR image of a human head (96) (see fig. 3). Since then considerable improvements have been made in NMR imaging of both the head and body, with no plateau in the rate of improvement in sight (see fig. 4).

BASIC TECHNICAL BACKGROUND

An understanding of nuclear magnetic resonance (NMR) requires a familiarity with certain natural phenomena. The first phenomenon is that all atoms, of which everything in nature is made, contain nuclei which, in turn, are made up of particles called protons and neutrons. It is these atomic nuclei to which the "N" in NMR refers.

The second natural phenomenon pertinent to an understanding of NMR is that certain nuclei, namely those that contain an odd number of protons, or an odd number of neutrons, or both, possess an intrinsic angular momentum, called "spin." Since nuclei are electrically charged, those nuclei that spin generate tiny magnetic fields. That is, they are magnetic. Only those nuclei that are magnetic, such as ^{1}Hydrogen, ^{13}Carbon, ^{19}Flourine, ^{23}Sodium, and ^{31}Phosphorus, can be exploited in NMR experiments. It is this phenomenon of nuclear magnetism to which the "M" in NMR refers.

Supplying radiofrequency energy of the appropriate rotational frequency will excite hydrogen nuclei from a lower energy level, E_1, to a higher

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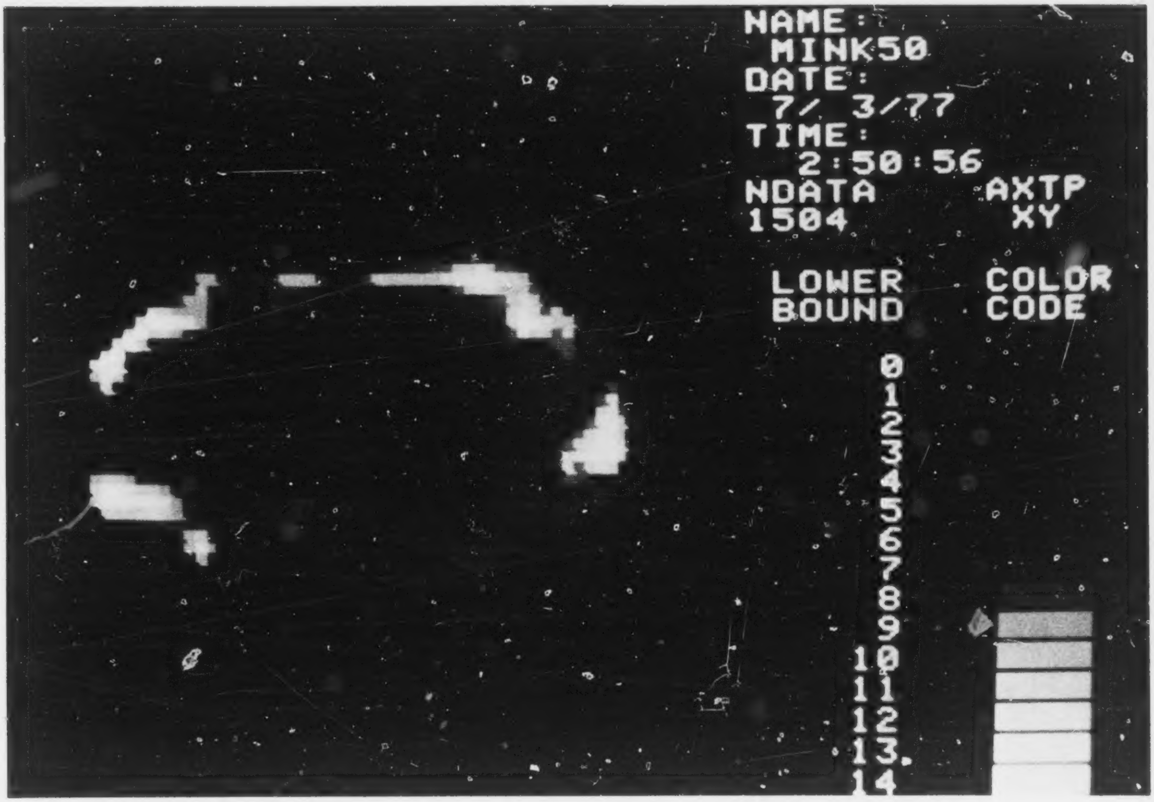
[3] The radiant energy used for NMR is low-frequency, non-ionizing radiofrequency waves, not the high-frequency waves used in X-rays.

Figure 2.—First In Vivo Human Whole-Body NMR Scan



SOURCE: Provided by Raymond Damadien, President, FONAR Corp.

level, E_2. If the radiofrequency energy is turned off after the nuclei have been raised into the higher energy level, the excited hydrogen nuclei drop back down to level E_1, i.e., they relax. In the process of relaxing, the hydrogen nuclei re-emit the energy they had initially absorbed. If this radiofrequency energy is repeatedly applied, hydrogen nuclei will oscillate, or resonate, back and forth between E_1 and E_2, alternately absorbing and emitting energy. It is this type of radiofrequency-induced resonance to which the "R" in NMR refers.

Since the NMR signals that are emitted by magnetic nuclei are extremely weak, atoms must be present in sufficient concentration in order to produce an NMR signal that is strong enough to be converted into an image exhibiting clinically useful spatial discrimination. To date, the nucleus of the hydrogen atom, which is the most prevalent in the body and has a single unpaired proton, has been most commonly exploited to produce high-quality NMR images.[4]

As Raymond Andrew has explained in his review of NMR imaging (8), NMR images are spatial representations of NMR signals. Although the signal detected in proton imaging is proportional to proton density, the image is not just a two-dimensional representation of that proton density. Rather, the signal also depends on three other parameters.

The first parameter is the velocity with which fluid is flowing through the structure being imaged, since the movement of protons in that fluid

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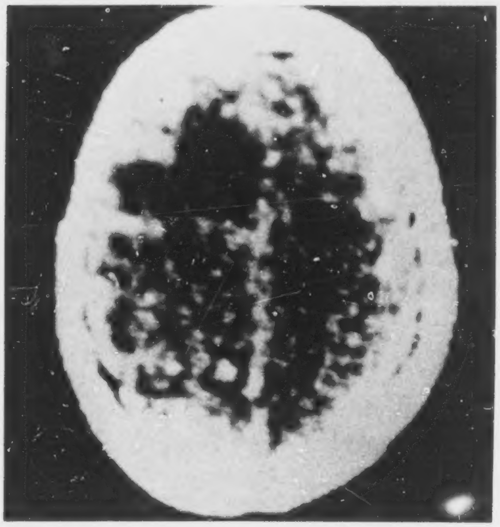
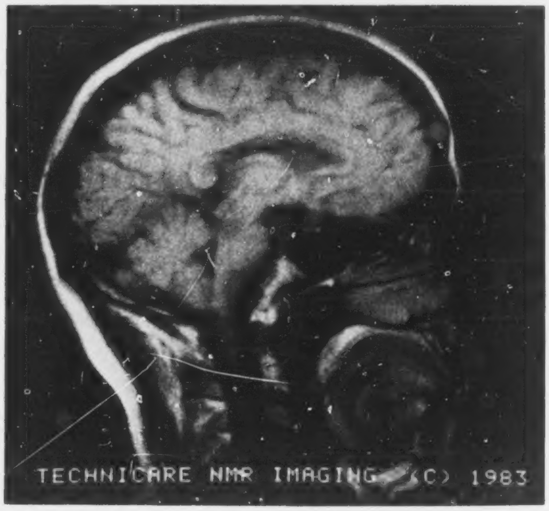
[4] Recently, sodium and phosphorus have also been imaged in some research centers.

Figure 3.—First NMR Image of a Human Head



SOURCE: G. N. Hounsfield, "Computed Medical Imaging" (Nobel Lecture, Dec. 8, 1979), *J. Comp. Assist. Tomog.* 4 (5):655-674, 1980.

Figure 4.—1983 NMR Image



SOURCE: Technicare.

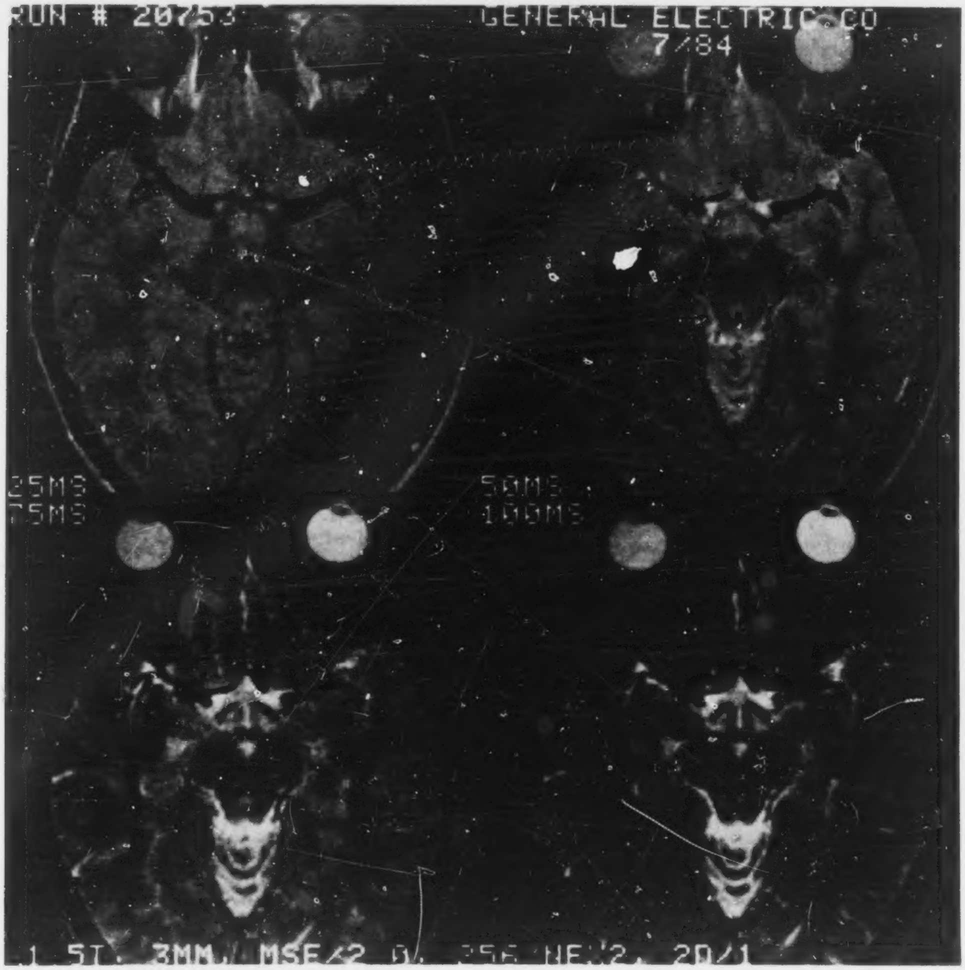
affects the intensity of the signal being detected. The other two parameters that affect an NMR image relate to the rate at which nuclei excited during an NMR study relax. The first relaxation parameter, called the "spin-lattice" relaxation time, or T_1, is a time constant that reflects the rate at which excited protons exchange energy with the surrounding environment. The other, called "spin-spin" relaxation time, or T_2, is a time constant that reflects the rate of loss of coherence (the rate at which protons stop rotating in phase with each other) due to the local magnetic fields of adjacent nuclei. Naturally occurring variations in relaxation times may have biomedical significance.

The extent to which any single NMR image reflects each of these four parameters (proton density, flow, T_1, and T_2) depends on the particular radiofrequency pulse sequence employed to excite the protons in a region being imaged (see app. A). Thus, there is no such thing as a unique NMR "picture" of any region of the body. Rather, as is illustrated in figure 5, NMR images of a single region vary depending on the pulse sequence used to produce them.

NMR images thus are fundamentally different from computed tomographic (CT) X-ray images. Whereas the latter rely on the linear attenuation of ionizing X-radiation to produce images that reflect differences in the electron density and specific gravity of adjacent tissues, NMR images are formed without use of ionizing radiation and reflect fundamental physiochemical differences between adjacent tissues. It is from the belief that enormous clinical benefits might be derived from obtaining information at a nuclear level through NMR, that the excitement about and investment in NMR have arisen.

Except for the addition of a computer and a system for producing a magnetic field gradient, the basic components used in modern day NMR imaging devices (see figs. 6 and 7) are qualitatively similar to those employed in the first NMR experiments performed by Bloch and Purcell in 1946. These components include: 1) a *magnet* whose aperture or bore (diameter) is large enough to enclose the structure being imaged (the magnet is used to produce a highly uniform magnetic field around the structure being imaged); 2) a set of *gradient coils* to impose the magnetic field gra-

Figure 5.—An NMR Image (3 mm slice) of a Normal Head From an Axial View With Changes in Pulse Sequence



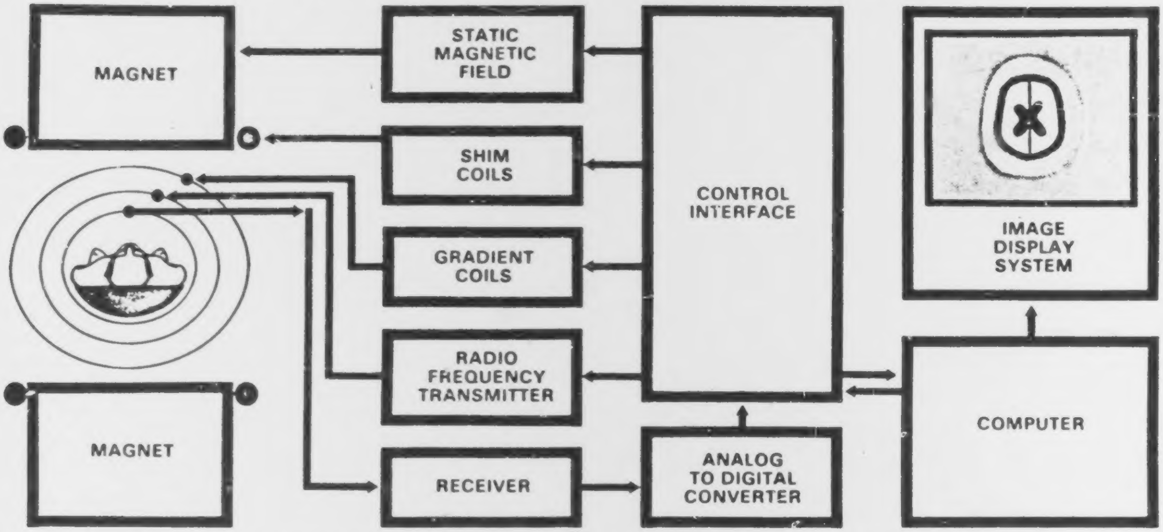
SOURCE: General Electric Co., 1984.

dient required to provide the system with spatial discrimination; 3) a *radiofrequency transmitter* to produce radiowaves that excite the nuclei being imaged; 4) a *radiofrequency receiver* to detect the radiofrequencies being emitted by excited nuclei during the process of relaxation; 5) a *computer* to control instrument operation and to reconstruct and store the image produced from the NMR frequency signals being detected; and 6) a display system.

MAGNETS

Although small-bore magnets had been employed in conventional NMR spectroscopy for many years, it was not until interest in NMR imaging emerged in the 1970s that magnets with bores large enough to accommodate a human being were designed and built. Much of the recent research and development on magnets for NMR imaging and in vivo spectroscopy has been funded

Figure 6.—Schematic Diagram of NMR Scanner Instrumentation



SOURCE: C. L. Partain, R. R. Price, J. A. Patton, et al. "Nuclear Magnetic Resonance Imaging," in Radiological Society of North America, Inc., 1984, figure 11, p. 13. (Courtesy of C. L. Partain).

in part by the NMR imaging industry and carried out by magnet manufacturers. The design of magnets manufactured specifically for NMR imaging, however, is still in an early stage of evolution, with improvements likely to be made as interest intensifies.

There are four main characteristics of magnets used in NMR scanners with which one should have some familiarity: magnet type, field strength, bore size, and homogeneity of field.[5]

Magnet Type

Two different classes of magnets can be used to produce the static magnetic field employed in an NMR scanner: electromagnets (either resistive or superconductive) or permanent magnets. Resistive magnets use electric current carried by copper or aluminum wire to create a magnetic field. Because copper and aluminum offer resistance to the flow of electric current, power must be supplied to force current through the wire. Energy supplied to power the system is lost as heat, requiring employment of a cooling system (usually cold water). Resistive magnets are comparatively light and inexpensive, and, because they can be shipped in parts, the costs of installing them are comparatively less than that for superconductive magnets. Resistive magnets do have high power requirements (50 to 100 kilowatts) resulting in operating costs of about $20,000 per year (6), however, and field strength is limited by cooling considerations to about 0.15 tesla[6] (126).

Superconductive magnets also utilize electric current to create a magnetic field, but instead of employing resistive materials such as aluminum or copper wire to carry the current, they use wire made from superconductive materials such as niobium-titanium alloys. Such alloys offer no resistance to current flow when operated at temperatures near absolute zero (126). In contrast to a resistive magnet, a superconductive magnet does not require an external source of electrical energy to sustain current flow once it has been started, as long as temperatures are maintained near absolute zero (126). Cooling of superconductive magnets is accomplished through use of liquid helium and liquid nitrogen. Helium needs to be replen-

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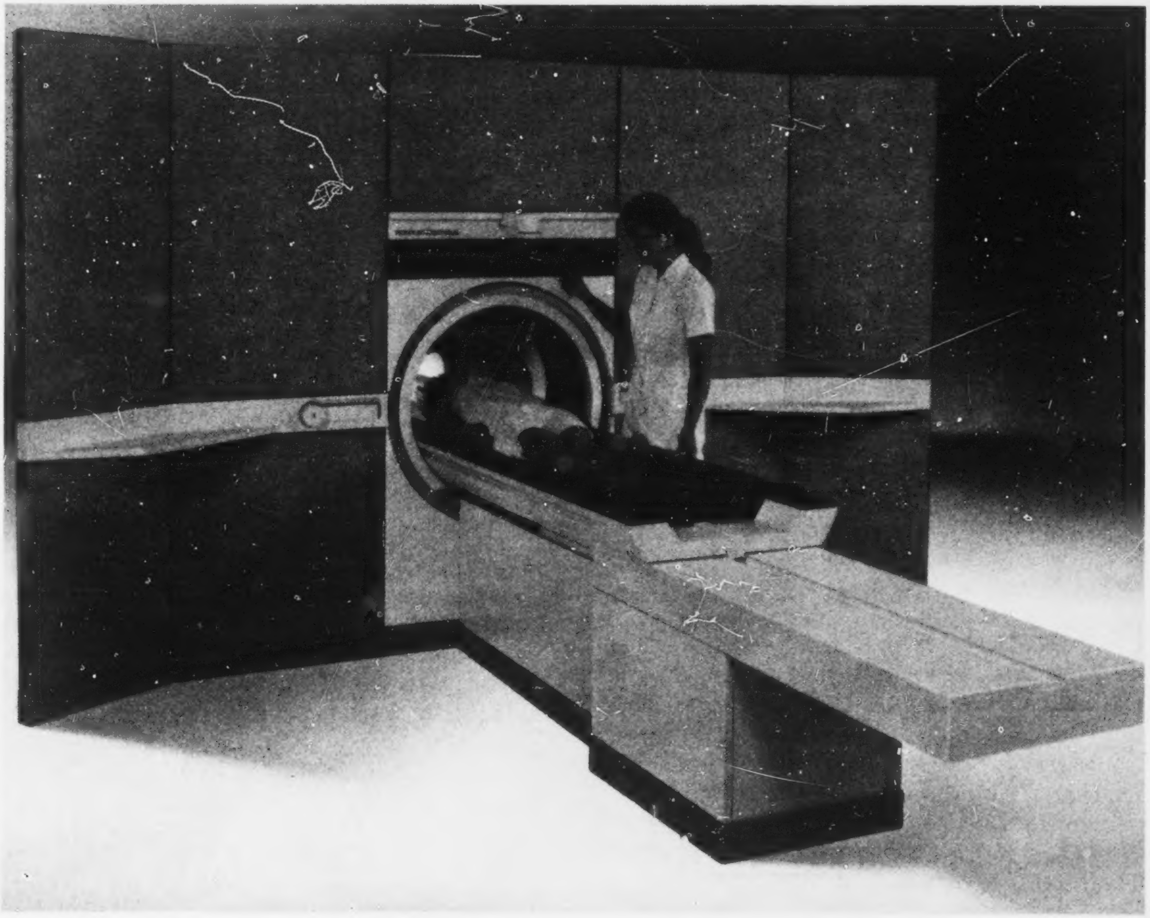
[5] Individuals interested in more than the following brief description of these features can consult standard physics texts or reviews written about magnets used in NMR imaging systems (57,126).

[6] Magnetic field strengths are measured in units of tesla (T). 1 T = 10,000 gauss (10 kilogauss). For perspective, the magnetic field strength of the Earth is approximately half a gauss.

Figure 7.—Modern Day NMR Imager



SOURCE: Picker International.

ished approximately once per month, whereas nitrogen needs to be replenished every one to two weeks.

Manufacturers are developing systems to reduce the loss, and therefore expense, of these coolants. Considerable research, for example, is being directed at development of techniques for recycling and liquefying the helium that now boils off into the atmosphere. In the event of excessive helium boil off, a superconductive magnet can quench (i.e., lose its superconductive properties). At least a day can be required to recool the magnet, during which time the instrument is unusable (126). The primary advantage of superconductive magnets is that they can carry high current densities, enabling generation of very high magnetic field strengths (see "Field Strength" below). Superconducting magnets can also provide magnetic fields that are both highly uniform and stable, once equilibrium is established.

Probably the most serious problem associated with use of resistive or superconductive magnets for NMR imaging derives from the external magnetic fields produced by the magnets and disruptions in the magnet's magnetic field produced by ferromagnetic objects (e.g., passing vehicles or elevators) in the vicinity of the magnet. The fringe field produced by electromagnets can erase magnetic tape and disrupt pacemakers. Magnetic objects in the environment, in turn, can cause unacceptable distortions in the primary magnetic field that degrade image quality. Because of these potential distortions, expensive preventive site preparation or renovation is necessary.

Problems related to stray magnetic fields do not occur with permanent magnets (126), resulting in fewer siting problems with the installation of permanent magnets. Because permanent magnets eliminate the need for either electrical power or liquid helium, they also have the advantage of lower operating costs. Permanent magnets tend to be extremely heavy (as much as 100 tons), however, often creating a need for reinforced floors. The field strength of most currently available permanent magnets does not exceed 0.3T.

Field Strength

The optimum field strength for proton NMR imaging is the subject of intensive research and debate. It is likely that no one field strength will be optimum for all NMR applications. Higher field strengths might be preferable to lower ones because a higher field strength increases the NMR signal/noise ratio, and increased signal to noise translates directly into improved image quality, finer spatial resolution, or reduced scan times, all other parameters being equal (21). Still at issue, however, is whether improvements in image quality achieved through increases in field strength above 0.3T will result in clinical benefits.

Bore Size

The size of specimens that can be imaged with NMR is limited by the diameter of the magnet bore. Whole body NMR scanners therefore require magnets with an effective bore diameter sufficient to accommodate a human body. Approximately 1 to 3 percent of patients that have been imaged to date have complained of feeling claustrophobic in the magnet.

Homogeneity of Field

Inhomogeneities in the magnetic field (lack of uniformity in magnetic field strength) can result in clinically important distortions in NMR images. As mentioned previously, both stationary and moving ferromagnetic objects can produce such inhomogeneities in the fields of resistive and superconductive magnets. Many of these problems can be minimized (albeit at significant expense) by magnetic field shimming (adjustments such as addition of special coils made to eliminate inhomogeneities in the magnetic field) and appropriate site renovations. Higher degrees of field homogeneity are required to perform ^{31}P spectroscopy than to perform proton imaging.

3.

Clinical Applications of NMR

3.
Clinical Applications of NMR

INTRODUCTION

When a new imaging modality is evolving as rapidly as NMR imaging, it is impossible to publish a review that accurately describes the "current status" of its clinical use. By the time such a review is published, it is out of date. Therefore, the goals of this chapter are: to provide a "snapshot" view of the state of the clinical applications of NMR in mid-1983 and to attempt to put the current status of various clinical applications into perspective, highlighting current limitations as well as advantages and distinguishing between potential applications and those that have been demonstrated with scientific rigor. More detailed clinical reviews are available (see, for example, 27,86,125,137,142,148,166).

The first section in the chapter provides a brief overview of potential biological hazards of NMR. The rest of the chapter is organized around the three clinical applications of NMR in which the most research had been performed as of this writing: 1) imaging of protons to assess normal and abnormal structure, metabolic processes, and fluid flow; 2) use of proton relaxation times[1] in the diagnosis of disease; and 3) use of the chemical shift phenomenon to assess biochemical processes in vivo (in vivo spectroscopy).[2]

The second section provides a clinical overview of proton (hydrogen) imaging, briefly summarizing results of research on proton imaging of the brain, mediastinum, hilum, lung, heart, breast, abdomen, kidneys, pelvis, musculoskeletal system, clinical oncology, and blood vessels. Readers without clinical background may wish to skip the second section and proceed directly to the third section (*Putting Proton NMR Imaging Into Perspective*), which discusses the advantages and disadvantages of NMR imaging and addresses a number of clinical and practical issues which help put the status of proton imaging into perspective. Section 4 (*Relaxation Parameters*) provides a brief overview of research relating to the clinical use of measurements of proton relaxation times. Again, readers without clinical or scientific background may want to skip this section and proceed directly to section 5 (*Putting T_1 and T_2 Relaxation Times Into Perspective*), which discusses the conclusions to be drawn from the research described in section 4. Finally, sections 6 and 7 briefly address in vivo spectroscopy. Non-scientists may wish to read only section 7, which attempts to place the current status of in vivo spectroscopy into perspective.

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[1] These relaxation times are estimated from NMR images.

[2] Imaging of nuclei other than hydrogen, such as sodium or phosphorus, has recently been accomplished, but is not included in this list. A discussion of the accumulated experience with such imaging is beyond the scope of this case study.

POTENTIAL BIOLOGICAL HAZARDS OF NMR

One of the primary advantages of NMR imaging is that it does not employ X-rays. Although there is thus no safety concern regarding X-irradiation with NMR imaging. concern has arisen regarding other potential hazards associated with use of NMR.

NMR safety concerns have focused on three NMR parameters: 1) time-varying magnetic fields, 2) radiofrequency electromagnetic fields, and 3) static magnetic fields.

Although the possibility exists that time-varying magnetic fields could induce electric currents that could cause ventricular fibrillation, cardiac arrest, inhibition of respiration, or tetanization (sustained muscular contraction), none of these potential adverse effects has been observed in over 2,000

NMR studies performed in England (179). Nor have significant problems relating to local heating induced by radiofrequency pulses, or pathological, developmental, genetic, or behavioral hazards caused by prolonged exposure to static NMR fields been observed (161). In fact, the only complications reported at a July 1983 FDA Radiologic Devices Panel meeting by Professor Robert Steiner, of Hammersmith Hospital, London, in his discussion of the British NMR studies, were that one baby had vomited and aspirated during positioning in the NMR scanner and that 3 percent of the subjects had opted out of having an NMR scan secondary to development of a feeling of claustrophobia when positioned in the magnet. Other centers have reported claustrophobic feelings in 1 percent of subjects (147).

Potential nonbiological hazards include projectiles of metallic objects in the vicinity of NMR magnets and damage to computer tape or other objects in the surrounding environment.

The unblemished NMR safety record is perhaps related to the extreme caution that has been exercised by clinical researchers working with NMR. Researchers have, for example, tended to exclude from their studies patients in whom cardiac pacemakers, large pieces of metal (such as an artificial hip), metallic cranial aneurysm clips, or metallic intrauterine devices have been implanted. Pregnant women have also tended to be excluded. It is possible that these restrictions will be relaxed in the future. For now, however, no harmful effects have been associated with NMR imaging under existing conditions of use.

In 1980, Great Britain's National Radiological Protection Board (NRPB) issued interim safety guidelines pertaining to NMR imaging of humans (table 1); revised guidelines are expected to be published soon. In 1982, the U.S. Food and Drug Administration (FDA) also issued guidelines, but FDA's guidelines were intended only to assist Institutional Review Boards in making decisions regarding what constituted "significant risk."

Table 1.—Suggested Guidelines for Safe Operation of NMR Imagers

	National Radiological Protection Board (U.K.) 1980[a]	Bureau of Radiological Health (FDA) (USA) 1982[b,c]
Static magnet field (tesla) (whole or partial body exposure)	<2.5 T	<2 T
Time-varying magnetic fields (whole or partial body exposure)	<20 T/sec for pulses for ≥10 msec	<3 T/sec
Radiofrequency electromagnetic fields	<15 MHz (<70 W average power absorbed)	≤0.4 W/kg[d] averaged over whole body; <2 W/kg over any one gram of tissue

[a] R. D. Saunders and J. S. Orr, "Biologic Effects of NMR," in *Nuclear Magnetic Resonance (NMR) Imaging*, C. L. Partain, A. E. James, F. D. Rollo, et al. (eds.) (Philadelphia: W. B. Saunders, 1983).

[b] W. E. Gundaker, *Guidelines for Evaluating Electromagnetic Risk for Trials of Clinical NMR Systems*, FDA Bureau of Radiological Health, Division of Compliance, Feb. 25, 1982.

[c] The NRPB guidelines specify upper limits that must not be exceeded. The FDA guidelines, in contrast, are intended to serve as an aid for Institutional Review Boards making determinations of what constitutes "significant risk" under an Investigational Device Exemption. Thus, the FDA does not prohibit use of NMR imagers that operate outside these recommendations.

[d] Average specific absorption rate rather than fixed frequency.

Some attempts are underway to maintain records of individuals who have undergone NMR imaging studies so that they can be contacted in the future. The NRPB is collating this type of exposure record, and the NMR Commission of the American College of Radiology has distributed patient data forms that are to be completed each time a patient undergoes an NMR imaging study. It would be advisable to establish uniform guidelines for collection of this type of data worldwide, at least for the near future. Who should be responsible for collecting and maintaining such data and who should bear the expense need to be determined. In addition, patient confidentiality issues need to be resolved.

PROTON IMAGING: A CLINICAL OVERVIEW

Brain

Thus far, the widest and most efficacious use of clinical proton NMR imaging has been for the brain and central nervous system. NMR's prowess in demonstrating the anatomy of the central nervous system derives in large part from two facts. First, although the proton density in the gray and white matter of the brain is approximately equal, gray matter contains approximately 15 percent more water than white matter. This difference in the chemical environment in which gray and white matter protons exist, which is reflected in differences in the T_1 relaxation time of gray and white matter, results in a significant level of gray versus white matter contrast in NMR images (30,52). This differentiation is much more striking with NMR imaging than with X-ray computed tomography (CT) because X-ray CT's linear attenuation coefficient for gray matter is only slightly different from that for white matter (24). Second, because cortical bone has a very low NMR signal strength, it is possible to image with NMR areas such as the posterior fossa, brain stem, and spinal cord that are not well seen by CT because the skull and vertebrae are impervious to the X-rays used in CT (136). In work done in Aberdeen, Scotland (166) and at Hammersmith Hospital in England (30), for example, NMR has produced clear images of the cerebellum and brain stem, and has demonstrated brain stem hemorrhages and cerebellar tumors not seen with CT.

NMR also appears to be more sensitive than X-ray CT to the demyelinating lesions that occur in multiple sclerosis (207).

In a report on cranial NMR scans performed on 140 patients with a broad spectrum of neurologic diseases and on 13 healthy volunteers, Bydder, et al., demonstrated NMR's ability to detect tumors, hemorrhages, infarctions, and ventricular size (30). It remains to be seen whether NMR will be superior to X-ray CT in demonstrating these types of pathologies in areas of the brain other than the posterior fossa and brain stem.

One final interesting central nervous system application of NMR is the study of brain development. Researchers at Aberdeen and Hammersmith, for example, have begun to explore the time course of myelination in newborns (166,178). Given the presumed safety of NMR imaging, further studies can be anticipated.

Mediastinum, Hilum, and Lung

Although recent evaluations of NMR imaging of the thorax suggest that the technique may prove useful in assessing mediastinal, hilar (referring to the anatomic area where the bronchus blood vessels, nerves, and lymphatics enter or leave the lung), and lung abnormalities (71,166), the data are still insufficient for comparing the efficacy of NMR with other imaging techniques in evaluating these structures. The possibility exists that variations in the T_1 relaxation time between blood and soft tissues might permit clinically useful discriminations between blood, fat, and hilar tumors to be made without use of intravenous contrast materials. Clinical trials are necessary, however, to assess the sensitivity and specificity of NMR imaging in these applications. Early work at Aberdeen suggests that some peripheral lung tumors may not be so well seen with NMR as with X-ray CT (166). If this proves to be the case, clinicians might use X-ray CT to evaluate lung parenchyma and NMR to evaluate the hilum. Finally, the possibility of exploiting differences in relaxation times between flowing, static, and clotted blood suggests that NMR might be used to diagnose pulmonary emboli. Respiratory gating (a technique in which image acquisition is coordinated with the breathing cycle) may improve the diagnostic quality of all types of NMR studies of the lung.

Heart

Researchers have begun investigating the potential for using NMR to produce tomographic images of the heart muscle, chambers, and valvular structures (27,43,56,83,142). Although the spatial resolution in images of the heart obtained to date is crude compared to that of images of the brain, advances in cardiac imaging are being made as techniques for gating of images to the electrocardiogram are developed (114) and refinements are made in the application of high-speed imaging techniques (such as the echo-planar technique—a particular type of NMR imaging in which an image of a plane is obtained from an excitation pulse) (124) to visualization of the beating heart (27,142). Although NMR tomographic imaging of the anatomical structures of the heart must for now be considered experimental, evidence is accumulating that NMR may emerge as the modality of choice in the imaging of certain structures. (See, for example (176), relating to imaging the pericardium with NMR versus X-ray CT.)

Another potential cardiac application of proton NMR imaging is discrimination between infarcted, ischemic, and normal myocardium (27,142). In early work performed at Massachusetts General Hospital, researchers were able to distinguish ischemic from non-ischemic canine myocardium with, but not without, use of a paramagnetic (a substance with a small but positive magnetic susceptibility (magnetizability) that may increase the contrast between tissues and NMR images) (4) contrast agent (76). Although manganese, the contrast agent used, may be too toxic to be used in humans, other less toxic paramagnetic agents might be developed (23,76). More recently, investigators at the Massachusetts General Hospital have used anti-myosin (antibodies directed against myosin, a component of muscle) monoclonal antibodies labeled with manganese and injected into the coronary arteries to visualize acutely infarcted myocardium in dogs (110). Finally, researchers at the University of California at San Francisco have been able to distinguish in vivo between normal tissue and experimentally induced infarcts in the lower extremities of rats within 24 hours of infarction (89). Further research needs to be performed before the implications of these findings to the diagnosis of myocardial ischemia and infarction in humans can be determined.

Breast

Ross, et al., reported on a series of NMR scans of 128 breasts examined in 65 patients (155). Scans were obtained using a magnetic field strength of 0.045 T. The investigators found that although normal breast tissue could often be distinguished from abnormal breast tissue, there was some difficulty in localizing abnormalities, as well as some degree of overlap of T_1 values obtained from benign and malignant breast tissues. The latter may limit NMR's diagnostic efficacy in this application.

Ross, et al., also cited the prolonged time required to do an NMR breast scan as a possible limitation of the technique (at a relatively low magnetic field strength). In Ross' study, the average total examination time per patient was 1 hour. Pairs of transverse sections of the breasts were produced in 10 minutes; T_1 measurements were made in 6 minutes. The average total examination time per patient exceeds the time required to produce individual transverse sections because images of several sections are used in the process of completing a patient examination.

Yousef, et al., employing a 0.3 T superconducting magnet, recently reported experience with NMR imaging of two patients with breast abnormalities (58). Three-dimensional NMR images in one case and single-slice planar images (images taken through a single plane) in the other correlated well with mammograms performed in the same patients. The authors suggest that NMR imaging may prove useful as a noninvasive probe of breast lesions, but acknowledge that it is premature to predict the efficacy of NMR in the assessment of human breast disease (58).

Abdomen

Although the T_1 values of the major abdominal organs are sufficiently specific to make recognition of those organs relatively easy with proton NMR imaging, there may not be sufficient difference between the values in normal and diseased states to permit pathologic diagnoses to be made with a high degree of accuracy (166). Results of small clinical series of NMR imaging of the liver (53,132,167) and pancreas (169,175) have been reported, but further comparative studies need to be performed before the clinical utility of NMR imaging of space-occupying lesions in the abdomen can be defined.

There is some indication that metabolic liver disease may also be amenable to evaluation by hydrogen NMR imaging techniques. NMR can be used to measure liver iron overload in patients with hemochromatosis (173), for example, and to demonstrate focal areas of inflammation in patients with chronic active hepatitis (174).

Kidneys

Although several studies of proton NMR imaging of the kidney have been reported (98,118, 168,170), NMR investigations of the anatomy and function of the kidneys must be considered experimental at this time. The possibility of distinguishing between renal cortex and medulla with NMR (98) has been demonstrated, but further studies are needed before the clinical utility of such NMR data can be defined. Similarly, NMR's role in the clinical evaluation of renal diseases such as glomerulonephritis remains to be demonstrated (98). One potential disadvantage of using NMR to evaluate the kidney is its inability to detect calcifications. In another area, Ackerman, et al., have begun exploring the possibility of employing NMR to evaluate transplanted kidneys (2).

Pelvis

Researchers at Aberdeen were able to correctly differentiate between benign prostatic hyperplasia and prostatic carcinoma with proton NMR in 27 of 30 men with symptoms of urethral obstruction. Two cases, however, were misdiagnosed as cancer when, in fact, prostatitis was present (166), again illustrating that pathologic diagnoses made with proton NMR may not be sufficiently specific to obviate the need for biopsy. Bladder tumors have also been imaged (178). It is too early to assess the utility of using NMR in the staging of cervical, uterine, and ovarian cancer. The fact that NMR imaging does not employ ionizing radiation, however, makes it attractive as a potential means of imaging the pelvis, particularly in children and pregnant women. More recent developments in NMR imaging of the pelvis have been reviewed elsewhere (97).

Musculoskeletal System

Although NMR does not visualize bone cortex, it can be used to demonstrate bone marrow and alterations in bone architecture. Consequently NMR has been used to demonstrate osteomyelitis and tumor metastases in vertebral bodies and pelvic bones (166). Because of its ability to provide sagittal and coronal images, NMR may prove useful in examination of the spinal canal, but again studies comparing NMR to other techniques need to be performed before NMR's role in this regard can be defined. Early work has suggested that both the spinal cord and nucleus pulposus can be discerned in NMR images. Images of muscles, tendons, and ligaments demonstrating great detail have also been produced with NMR (131), suggesting that NMR imaging is likely to prove valuable in the evaluation of musculoskeletal disorders.

Clinical Oncology

As has been discussed, further research needs to be performed before the role of proton NMR imaging in the diagnosis of cancer can be defined (14). Additional techniques need to be developed before NMR can be used to distinguish with clinically useful accuracy between benign and malignant lesions. Because NMR does not employ ionizing radiation, it might be used frequently to closely monitor the progress of pediatric and adult cancer patients being treated with radiation or chemotherapy. Finally, the exciting possibility exists, but remains to be demonstrated, that NMR could prove capable of detecting malignant abnormalities at a stage earlier than is currently possible. If that potential is realized, the additional possibility exists that clinicians will become more successful in treating the malignancies that are detected.

Blood Vessels and Flow

NMR imaging offers two different approaches to the evaluation of vascular disease. Although it is still too early to assess the sensitivity and specificity of NMR techniques in the detection of vascular obstructions, a number of investigations have suggested that proton NMR imaging can be used not only to demonstrate atherosclerotic vascular disease, but also to qualitatively assess flow in major vessels (3,41,81,108,109). These findings are particularly interesting since NMR imaging does not require the potentially toxic radiopaque dyes and catheterization of traditional angiography.

PUTTING PROTON NMR IMAGING INTO PERSPECTIVE

NMR imaging has captured the interest of the medical profession for a number of reasons. First, it eliminates the risk of X-radiation exposure that is associated with use of devices such as X-ray CT scanners. Second, in addition to providing excellent spatial resolution (on the order of 1.0 millimeter), the technique provides excellent contrast resolution without the need for injection of potentially toxic contrast agents. Third, because of the absence of NMR signal artifact from bone, physicians can visualize areas such as the posterior fossa, brain stem, and spinal cord with NMR that were not well seen with other noninvasive imaging modalities. Finally, because NMR images are sensitive to fundamental physical and chemical characteristics of cells, the technique offers the *possibility* of detecting diseases at earlier stages than is currently possible and of permitting accurate pathologic tissue diagnoses to be made noninvasively. These and other potential clinical or practical benefits associated with NMR imaging are summarized in table 2.

NMR imaging is not without its disadvantages, however (see table 3). NMR imagers, for example, are expensive and their installation is costly and difficult. In addition, the magnetic fields used to generate NMR images with resistive and superconducting systems are sensitive to radiofrequency interference and may damage computer tape or other objects in the surrounding environment. Furthermore, it is currently thought not to be safe to perform NMR imaging on certain patients (e.g., those with pacemakers or metal implants, such as aneurysm clips). Finally, until more experience with the modality is obtained, NMR imaging may require more *physician* time in performance of patient examinations than X-ray CT or other imaging modalities.

Table 2.—Demonstrated and Potential Advantages of NMR Imaging

A. Demonstrated benefits

1. Uses no ionizing radiation; currently free of known biological hazards
2. Sensitive to differences in proton density and relaxation parameters, providing a basis for a high degree of soft tissue contrast
3. Does not require injection of potentially toxic contrast agents (In the future paramagnetic contrast agents may be developed for use with NMR. The risk associated with use of such agents will have to be evaluated.)
4. Low-intensity signal from bone, resulting in improved visualization of the posterior fossa, brain stem, and spinal cord
5. Can produce three-dimensional as well as tomographic images in virtually any imaging plane without reformatting (computer manipulation of the image)

B. Potential clinical or practical benefits

1. Increased sensitivity to physicochemical characteristics of tissues may permit enhanced detection of disease (if, for example, alterations in tissue physicochemical character can be detected prior to alterations in organ function or morphology)
2. Increased sensitivity to physicochemical characteristics of tissues may permit accurate pathologic tissue diagnoses to be made noninvasively (The development of nontoxic paramagnetic contrast agents would be particularly useful in this regard.)
3. Potential for analysis of flow of blood and other fluids, such as cerebrospinal fluid
4. Absence of moving parts may decrease maintenance costs and increase the useful lifetime of NMR imagers

SOURCE: E. P. Steinberg, Johns Hopkins Medical Institutions, Baltimore, MD, 1983.

Table 3.—Current and Potential Disadvantages of NMR Imaging

A. Current disadvantages

1. NMR imagers are expensive
2. Difficult and expensive site preparation
3. Exclusion of patients with pacemakers; metal implants, such as aneurysm clips; or claustrophobia. (Patients who have undergone brain surgery in whom there is uncertainty regarding whether metal clips were implanted may need to be X-rayed before being imaged with NMR. Metal detectors are also being used.)
4. Insensitivity to dense bone and calcifications
5. Relatively prolonged acquisition times and sensitivity to motion result in degradation of images of moving anatomic structures

B. Potential disadvantages

1. May require more physician time in performance of patient examinations compared to other imaging modalities
2. Examination times could prove to be longer than with X-ray CT or ultrasound, resulting in fewer patients examined and increased average cost. (Newer developments in imaging techniques may change this)

SOURCE: E. P. Steinberg, Johns Hopkins Medical Institutions, Baltimore, MD, 1983.

Because the number of clinical applications of NMR imaging and the utility of each is constantly evolving (table 2), NMR's role in medicine has yet to be determined. As Kaufman, Tosteson, et al., have pointed out, many of the claims that NMR will provide detailed chemical information specific enough to be diagnostically useful are premature (109). Although there is some plausibility to the hundreds of applications that have been cited for NMR, the majority of such applications must be considered *potential* rather than *demonstrated*. Although T_1 and T_2 relaxation times have been found to vary in different pathologic processes, for example, researchers have so far been unable to characterize tissue pathology as specifically as had originally been expected using T_1 and T_2 values. The possibility exists, however, that through the development of nontoxic paramagnetic contrast agents, much of the noninvasive diagnostic potential of NMR that had been hoped for can be realized.

Whether the results that have been observed in research institutions to date will be easily duplicated by other institutions remains to be seen. The NMR imaging that has been performed so far has taken place in research centers that possessed or acquired considerable background and expertise in NMR prior to initiation of an NMR imaging program. Most, if not all, such centers have utilized interdisciplinary teams consisting of physicians, physicists, engineers, and others to produce the images that have been published so far. In addition, the exquisite images that are helping to fuel excitement about NMR imaging have often required prolonged amounts of time that it may not be practical to expect most hospitals to expend. Although future NMR production models are likely to simplify image acquisition for the physician, and although the time required to produce high-quality images is likely to decrease, it should not be assumed that images of the same quality as those published or displayed to date will necessarily be produced *immediately* in hospitals that are not able to spend equivalent time and effort on their production.

Furthermore, although in most research studies performed to date several physicians have interpreted NMR scans independently and without access to comparative X-ray CT scans to guide them, in many, if not most, instances patients with *known* pathologies were being imaged. This is, of course, not only reasonable, but also advisable in the early stages of evaluation of a new technology. Nonetheless, NMR will not necessarily be shown to have the same sensitivity and specificity when used to image patients with unknown types of pathology.[3] (See (149), for example.)

Although researchers have reported the ability to produce head and body images with NMR in times comparable to those required for X-ray CT scanning (41), it is possible that the time required to perform NMR studies on patients with unknown types of pathology will be longer than that required by experts imaging patients with known pathology (table 3). Given the variability in NMR images depending on the pulse sequence employed, researchers are finding that certain pulse sequences are better for demonstrating one type of pathology, while different pulse sequences are better able to demonstrate other types of pathology. Optimal pulse sequences for different pathologies are therefore being sought. It is likely that in the future pulse-sequence algorithms that are best suited to imaging specific medical problems such as abscesses, hemorrhages, and tumors will be built into NMR software. Although this development implies improvement in NMR images of individual types of pathology, it also implies that patients with unknown types of pathology who are referred for a "screening" NMR scan in the workup of symptoms such as fever, weight loss, or pain will have to receive multiple scans using multiple pulse sequences to exclude an abnormality. Such use of multiple pulse sequences may increase the time required to perform NMR studies.

The relationship between pulse sequence and pathology suggests two additional issues. The first is the issue of how many different pulse sequences will have to be employed before an examining physician is comfortable with concluding that a patient is normal. The second is that unless examining physicians are thorough, existing pathology may be overlooked. It is thus possible that a tension will develop between the economic pressure to maintain scheduling of a reasonable number of patients and the clinical requirement that pathologic abnormalities be excluded with a high degree of certainty. To the extent that the latter predominates, fewer patients may be seen, producing a rise in average cost per NMR study. To the extent that the former predominates, the sensitivity and specificity of NMR may decrease.

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[3] On the other hand, given the rapid improvements taking place in NMR imaging, current assessments may underestimate the ultimate sensitivity and specificity of NMR in many applications.

Finally, since NMR imaging employs no ionizing radiation, it is possible that patients can safely have repeated NMR scans over time to monitor therapeutic progress or the natural history of disease. To the extent that such monitoring is demonstrated to provide clinically useful information, the temptation to scan a single patient more frequently may increase. Such an effect would increase demands on NMR machines, which would result in hospitals' having to either ration time on NMR machines or purchase more NMR scanners. A second potential effect of "sequential scanning" is that in the absence of prospective payment (as is now the case for patients in many States), health care bills might increase (see ch. 8). The occurrence and magnitude of such increases depend on the extent to which sequential NMR scanning decreases or increases total patient management costs and improves patient care.

In conclusion, NMR imaging is a new modality thought to be capable of providing not only anatomic information comparable or superior to that obtainable with other imaging techniques, but also chemical and metabolic information that could yield noninvasive insights into tissue histology and function. Were NMR to be considered just another means of visually demonstrating anatomy, therefore, its true *potential* would be drastically underestimated. The lack of ionizing radiation or demonstrated hazard associated with NMR imaging, as well as the apparent lack of need to employ toxic contrast agents to obtain high-contrast images, would suggest an important clinical role for NMR imaging in medicine even if it proved to be no more efficacious than X-ray CT scanning. Considerably more research, such as that described in table 4, will be required before NMR's potential is determined and its most appropriate roles in clinical medicine are defined.

Table 4.—Likely Areas for Future NMR Research

1. Determination of clinical utility of NMR imaging compared to other imaging modalities
2. Improvements in magnet design (e.g., increased field uniformity; increased field strength; techniques for conserving liquid helium and nitrogen)
3. Determination of magnetic field strength that yields optimum image quality for hydrogen, for other nuclei, or for combinations of hydrogen and other nuclei)
4. Identification of pulse sequences optimal for demonstrating different types of pathologies
5. Improvements in imaging software and techniques affecting image quality, resolution, and scan time
6. Optimization of radiofrequency coils
7. Development of new and improved surface coils
8. Improvements in siting and shielding techniques
9. Development of paramagnetic agents for assessing tissue pathophysiology
10. Further development of whole-body spectroscopic techniques and applications
11. Imaging of nuclei other than hydrogen (e.g., sodium or phosphorus)

SOURCE: E. P. Steinberg, Johns Hopkins Medical Institutions, Baltimore, MD, 1983.

RELAXATION PARAMETERS

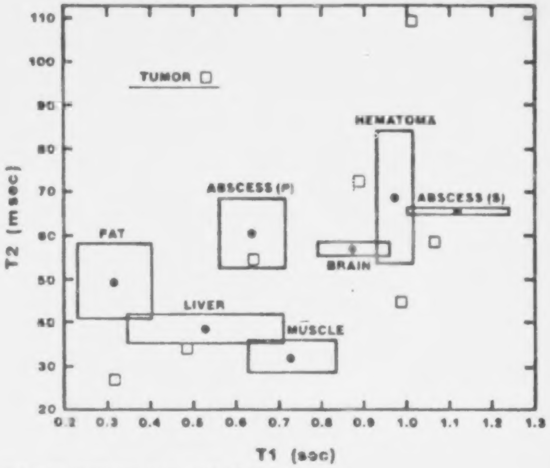
As has been mentioned previously, proton NMR images reflect not only the proton density of the tissues being imaged, but also the proton relaxation time characteristics of those tissues. In addition to exploiting these relaxation parameters to enhance the contrast of NMR images, researchers over the past decade have been investigating the extent to which quantitative measurements of T_1 and T_2 can be employed to make precise, yet noninvasive pathologic assessments.

The first indication that relaxation times might have diagnostic significance emerged from the early work of Raymond Damadian at the State University of New York, Brooklyn. In 1971, Damadian demonstrated that the proton spin-lattice relaxation time (T_1) in excised tumors that had been experimentally induced in rat livers was prolonged compared to the T_1 values of normal rat liver tissue (42). The T_1 relaxation times of two benign fibroadenomas were likewise found to be distinguishable from those of the malignant tissue (42). Similar results were observed by others shortly thereafter (32,84,93,160). In 1974, Damadian extended this work to humans, finding the T_1 values of 106 surgically excised human tumors to be longer than the T_1 values of the corresponding normal tissues (45,46). About the same time, Weisman and Bennett discovered that they could use NMR to differentiate in vivo between the normal tissue of a mouse's tail and a malignant melanoma transplanted into the tail (202).

Out of concern that experimental malignant tumors with slower growth rates might manifest T_1 values within the range observed for normal tissues of nontumor bearing animals, Hollis, et al., studied intermediate and slow-growing malignant tumors in rats (92). The authors found that the T_1 values of these more slowly growing tumors were again longer than those of normal rat liver, but overlapped T_1 values of other types of normal tissues (92). In view of this finding, Hollis and his co-workers voiced the concern that ". . . the overlap of T_1 values for malignant and normal specimens raises the possibility of confusion between primary tumors adjacent to sites of similar or higher T_1 value, or between normal tissue and metastatic tumors having a similar or lower T_1 value" (92).

Similar observations were subsequently made by others. Herfkens and co-workers at the University of California at San Francisco, for example, found that the T_1 values of in vivo tumors in rats estimated by NMR imaging techniques varied widely, and, although mean T_1 values of the tumors were high, individual T_1 values overlapped the full range of normal and other types of abnormal tissues (87). The same group also explored the possibility of using both T_1 and T_2 values estimated by NMR imaging techniques to distinguish between different types of pathologic abnormalities and found that contrast differentiation between normal and abnormal tissues was improved, albeit still imperfect (87) (see fig. 8).

Figure 8.—Mean and Standard Deviations for T_1 and T_2 of Various Tissues in a Live Rat



SOURCE: Herfkens, et al., 1981 (88).

PUTTING T_1 AND T_2 RELAXATION TIMES INTO PERSPECTIVE

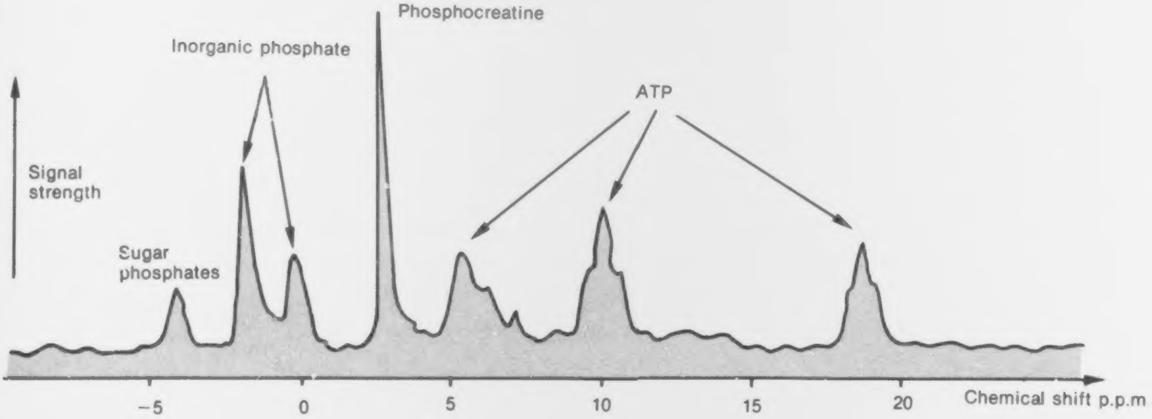
A number of conclusions can be drawn from the results of studies on the potential use of quantitative T_1 and T_2 values for pathologic diagnosis. First, within certain numerical ranges, relaxation times may provide sufficient pathologic specificity (to distinguish normal from abnormal, and one disease from another) to be clinically useful in understanding disease processes. Second, in instances in which overlap exists between the T_1 and T_2 values of normal and abnormal tissues, it will not be possible to use relaxation values alone to make reliable pathologic diagnoses, despite the theoretical attractiveness of doing so. Third, even if "natural" T_1 and T_2 values do not prove to provide the pathologic specificity that had been hoped, they may be useful in understanding disease processes. In addition, there is the possibility that nontoxic paramagnetic contrast agents (21,23,156) may modify relaxation properties and enhance diagnostic specificity. Fourth, the possibility exists, yet remains to be demonstrated, that detectable changes in T_1 and T_2 values may precede the development of noticeable anatomical changes in ways that will be clinically useful. Studies of early changes in T_1 and T_2 during oncogenesis, radiotherapy, and chemotherapy, for example, may provide immediate clinical dividends, as well as insights into the etiology of cancer and new modes of cancer therapy. Finally, considerable research remains to be done in the exploration of which physical, chemical, and biological factors give rise to and influence NMR relaxation times. Only through answers to these questions will it be possible to exploit relaxation times' full medical and scientific potential.

IN VIVO SPECTROSCOPY

Although small concentrations of phosphorus are present in the body, researchers have recently detected NMR signals from phosphorus of sufficient intensity to produce images. Researchers have also been able to perform in vivo phosphorous NMR spectroscopy in which the "chemical shift" phenomenon is used to indicate the relative concentrations of compounds such as phosphocreatine, adenosine triphosphatase (ATP), and inorganic phosphate in human tissues or organs (see fig. 9). Such a noninvasive metabolic probe has tremendous potential applications in medicine.

It has been demonstrated, for example, that levels of inorganic phosphate rise, while the concentration of phosphocreatine falls, in cells deprived of oxygen (165). The possibility thus exists that NMR spectroscopy could be employed not only to assess the utilization of ATP and the viability of oxygen-deprived brain or heart tissue (22), but also to gain insight into the functional and metabolic status of brain, heart, or peripheral muscle tissues in various physiologic and pathologic states. It has been demonstrated, for example, that the pH of oxygen-deprived tissue can be calculated from the positions of inorganic phosphorus peaks observed with NMR spectroscopy (22,26) and that changes in muscular metabolism during exercise can be detected by NMR (70,145). Rare diseases due to inborn errors of metabolism, such as McArdle's syndrome, can also be diagnosed using in vivo NMR spectroscopy (146).

Figure 9.—NMR Phosphorus Spectrogram[a]



[a] Graphic depiction of the individual components of NMR signals from phoshorus-containing compounds arranged according to the frequency of electromagnetic radiation.

SOURCE: D. I. Hoult, "An Overview of NMR in Medicine," U.S. Department of Health and Human Services, National Center for Health Care Technology, February 1981.

PUTTING IN VIVO SPECTROSCOPY INTO PERSPECTIVE

Much additional research is required before an assessment can be made of the extent to which in vivo NMR spectroscopy can be used to provide diagnostically useful clinical information regarding the metabolic and functional status of normal and abnormal tissues. It should also be recognized that the technology required for in vivo human NMR spectroscopy of organs such as the heart or brain is considerably more sophisticated than that required to perform proton NMR imaging. Superconducting magnets operating at high field strengths (on the order of 1.5 T or greater) with extremely high levels of field uniformity, for example, seem to be required to provide adequate resolution of the peaks emanating from various phosphorus-containing compounds. Thus most of the NMR imagers that are generally being installed in hospitals today (i.e., ones with field strengths less than 1.5 T) may not be capable of performing NMR spectroscopy. In addition, even though it has been proven feasible to perform spectroscopy on the 1.5 T imaging systems currently being installed, it is possible that neither proton imaging nor in vivo spectroscopy can be performed optimally at a field strength of 1.5 T.[4] Hospitals desirous of performing spectroscopy and imaging, therefore, may need either to obtain more than one NMR machine or be content to tolerate potentially costly periods during which field strengths are changed and the NMR machine is therefore not operational.[5] Considerably more research is also required before specialized equipment, such as auxiliary surface coils, are designed that permit NMR spectroscopy of phosphorus and other nuclei to be performed optimally. For the present, therefore, in vivo NMR spectroscopy should be considered an exciting and promising area of research that is of questionable feasibility for most hospitals.

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[4] High-quality images of both the head and body have recently been produced at 1.5 T. It is too early to know whether images produced at 1.5 T will be better or faster than those produced at lower field strengths.

[5] In addition, alterations in software may need to be made in association with adjustments in the field strength, and such software changes may prove to be too time-consuming to be practical.

4.
The NMR Imaging Device Industry

4.

The NMR Imaging Device Industry

INTRODUCTION

NMR imaging is fast emerging as the "growth" technology in the diagnostic imaging field. The possibility of unrivaled image quality, coupled with the perceived demand for a less risky alternative to X-ray computed tomography (CT) and radionuclide scanning, has led numerous firms to invest heavily in NMR imaging research and development. Since 1976, at least 23 companies worldwide have entered the NMR imaging marketplace. The industry is both dynamic and intensely competitive. Sales of NMR imaging devices over the next 5 years have been estimated by one source at $6.4 billion (60), an estimate that some manufacturers contend is conservative. The future of the industry, however, will depend not only on the internal composition and behavior of the industry, but also on external economic and regulatory forces, including Federal and State policies toward technology development and diffusion, and third-party decisions regarding payment. This chapter will focus on the NMR imaging industry, while succeeding chapters will address external economic and regulatory forces affecting that industry.

To understand the forces driving the NMR imaging device industry, it is necessary first to focus on three elements that have become standard in the analysis of American industry: structure, conduct, and performance (31). *Structure* refers to the composition and boundaries of an industry, i.e., the number and size distribution of its firms and their ability to enter the marketplace. *Conduct* pertains to the behavior of such firms once they gain entry to the marketplace, e.g., their policies toward setting prices, differentiating their products, and engaging in competition with one another. *Performance* relates to the results of firms' behavior, i.e., how well the industry is able to achieve recognized economic goals of efficiency and profitability. Industry structure often influences the nature of market conduct, which, in turn, may affect the quality of industry performance.

INDUSTRY STRUCTURE

The NMR imaging device industry may be examined through several important structural features, including seller and buyer concentrations, barriers to entry, diversification of firms, and acquisition and merger activity. The findings presented here reflect our own interpretations of data from multiple sources and do not represent the official views of the firms concerned. (A description of the methods employed in our survey of manufacturers appears as app. B; detailed descriptions of manufacturers, products, and clinical placements of NMR imaging units appear in app. C.)

Seller Concentration

The NMR imaging device industry may be divided into three groups of manufacturers, based on their stage of research and development (R&D) as of October 1983 (see table 5). Of the 20 firms for which we have information, seven had reached an *advanced* stage in which they had conducted extensive preproduction technical testing and had placed numerous units in clinical sites outside their factories. Each of these advanced stage firms had also developed a commercial prototype system[1] that was available for placement. Two companies, Diasonics and Technicare, obtained FDA premarket approval for the sale of their devices in March 1984, and a third, Picker International, in May 1984.

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[1] See subsequent discussion of industry development for definition of a commercial prototype system. By August 1984 Elscint had also reached the advanced stage. See app. C.

Table 5.—The NMR Imaging Device Industry, October 1983

Companies in advanced stage of development
Engineering model(s) complete; *multiple* clinical placements outside factory; ongoing clinical studies since 1982 or earlier; commercial prototype system(s) available for placement:
- Bruker Instruments
- Diasonics Inc.[a]
- Fonar Corp.
- Philips Medical Systems
- Picker International[a]
- Siemens Medical Systems
- Technicare Corp.[a]
- Elscint Ltd.[b]

Companies in intermediate stage of development
Engineering model(s) complete; *limited* clinical placements outside factory; generally *limited* clinical study thus far; commercial prototype system(s) generally *not* yet available for placement:
- General Electric Co.
- M&D Technology Ltd.[c]
- Toshiba Corp.

Companies in early stage of development: [d]
Engineering model(s) under development; *no* clinical placements outside factory; commercial prototype system(s) still to be defined:
- ADAC Laboratories
- CGR Medical Corp.[e]
- Fischer Imaging Corp.[f]
- Hitachi Ltd.
- JEOL USA
- Nalorac Cryogenics[g]
- OMR Technology[h]
- Sanyo Electric
- Shimadzu Corp.

[a] FDA granted premarket approval in spring 1984.
[b] In the advanced stage by August 1984 (see app. C).
[c] Had extensive clinical experience prior to formation of company.
[d] Two other firms that have announced plans to develop NMR imaging systems are Ansoldo SPA and Instrumentarium Oy.
[e] Engineering model complete, but clinical placement is not expected until 1984.
[f] Had been developing its own NMR imaging systems until acquired by Diasonics Inc. in May 1983.
[g] As indicated in app. C, Nalorac Cryogenics had two clinical placements by August 1984. However, these are small bore, high field strength systems that are currently being used for research purposes only.
[h] Acquired by Xonics Inc. in late 1983.

SOURCES: Interviews with manufacturers; American Hospital Association, 1983 (6); Boteler, 1983 (20); and "Imaging Equipment Sales Close In On $4 Billion Mark," *Diag. Imag.* 5(11):55-61, November 1983.

By October 1983 four firms had progressed to an *intermediate* stage of R&D in which engineering and experimental models had been completed, but commercial prototype systems had either not yet been developed or not yet been installed in clinical sites. The extent of clinical study also varied widely among these manufacturers. M&D Technology Ltd. had the benefit of clinical experience acquired by its founders at the University of Aberdeen (Scotland) prior to its incorporation, but it had yet to reach the advanced production prototype stage.

Nine other manufacturers could be characterized as engaged in early R&D work in October 1983. Of these, only one (CGR Medical Corp.) had completed an experimental prototype on which clinical testing was expected to begin in 1984. One firm, Fischer Imaging Corp., had been acquired (May 1983) by a manufacturer in the advanced R&D group, Diasonics Inc. Complete details on the future organizational structure of the two companies and their respective NMR imaging programs are not available at this time.

Industry Profile. The multinational character of the NMR imaging device industry is reflected in the 19 firms listed in table 6.[2] In October 1983, U.S. companies accounted for 37 percent of the total, while Japanese corporations comprised another 26 percent. Five other nations had entries in the world market: West Germany and Great Britain with two companies each; and France, Israel, and the Netherlands with one apiece.[3]

Thirteen of the manufacturers (68 percent) are public corporations, some of which are giants in other fields (General Electric, Hitachi, Philips, Sanyo Electric, Siemens, Toshiba). Of the six privately held firms, two are owned by small groups of investors (Nalorac Cryogenics, OMR Technology[4]), while three others are subsidiaries of major corporations (Picker International, Bruker Instruments, CGR Medical Corp.). M&D Technology Ltd. is a unique entity financed by a combination of private individuals and public trusts in Aberdeen, Scotland.

In terms of organizational structure, 11 NMR imaging device manufacturers (58 percent) are independent firms, seven (37 percent) are wholly owned subsidiaries, and one is the Medical Systems Division of a major public corporation (General Electric). Fifteen NMR manufacturers (79 percent) have multiple product lines. Some of these

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[2] Because Fischer has been acquired by Diasonics, we have excluded it from table 6.

[3] Two other firms that have announced plans to develop NMR imaging systems are Ansoldo SPA of Genoa, Italy, and Instrumentarium Oy of Helsinki, Finland.

[4] OMR Technology has recently been acquired by Xonics Inc., a publicly owned multiproduct firm in the United States.

Table 6.—The NMR Imaging Device Industry: Company Profile[a]

Company[b]	Ownership	Product lines (single or multi)	Organizational structure	Country
ADAC Laboratories	Public	Multi	Independent	United States
Bruker Instruments	Private	Multi	Subsidiary of Bruker Physik R.A.G	West Germany
CGR Medical Corp.	Private	Multi	Subsidiary of Thompson-Brandt	France
Diasonics Inc.	Public	Multi	Independent	United States
Elscint Ltd.	Public	Multi	Independent	Israel
Fonar Corp.	Public	Single	Independent	United States
General Electric Co.	Public	Multi	Independent[c]	United States
Hitachi Ltd.	Public	Multi	Independent	Japan
JEOL USA	Public	Multi	Subsidiary of JEOL	Japan
M&D Technology Ltd.	Private	Single	Independent	United Kingdom
Nalorac Cryogenics	Private	Single	Independent	United States
OMR Technology[d]	Private	Single	Independent	United States
Philips Medical Systems	Public	Multi	Subsidiary of North American Philips[e]	Netherlands
Picker International	Private	Multi	Subsidiary of GEC	United Kingdom
Sanyo Electric	Public	Multi	Independent	Japan
Shimadzu Corp.	Public	Multi	Independent	Japan
Siemens Medical Systems	Public	Multi	Subsidiary of Siemens A.G.	West Germany
Technicare Corp.	Public	Multi	Subsidiary of Johnson & Johnson	United States
Toshiba Corp.	Public	Multi	Independent	Japan

[a] As of October 1983. Two other firms that have announced plans to develop NMR imaging systems are Ansoldo SPA of Genoa, Italy, and Instrumentarium Oy of Helsinki, Finland.

[b] In alphabetical order.

[c] Medical Systems Division is responsible for NMR imaging R&D.

[d] Acquired by Xonics Inc. in late 1983. Information on the merger not available.

[e] North American Philips is a trust associated with N.V. Philips of the Netherlands.

SOURCES: Interviews with manufacturers; Dun & Bradstreet, *Million Dollar Directory, 1983*, Parsipanny, NJ, 1983; Moody's Investors Service, *Moody's Industrial Manual, 1982*, and *Moody's International Manual, 1982*, New York, 1982; and "Imaging Equipment Sales Close In On $4 Billion Mark," *Diag. Imag.* 5(11):55-61, November 1983.

have parent firms with products that extend beyond the boundaries of health care (see later discussion of diversification among firms). Of the three firms pursuing NMR imaging solely, all are independent, only one is publicly owned (Fonar Corp.), and all but one (M&D Technology Ltd.) are based in the United States (see table 6).

The number of employees engaged by each firm in NMR imaging-related work varies across the industry. Of the 12 companies for which such information could be obtained in August 1984, 4 had fewer than 50 full-time NMR employees, with 2 of these reporting NMR programs utilizing 10 or fewer full-time employees. At the other extreme, 8 firms reported program staffs (R&D plus administrative/marketing personnel) of 100 or more individuals, with one company (General Electric) employing over 500 persons.[5] Individuals with doctorates in physics, physical chemistry, and engineering comprise a substantial proportion of all full-time employees, ranging from at least 75 percent in the smallest firms to at least 12 percent in the NMR work forces of the largest companies.

Market Share. The traditional measure of seller concentration in an industry is the four-firm or eight-firm "concentration ratio," i.e., the combined market share of the top four or eight firms as reflected in their annual sales (31). Because NMR imaging units have been considered investigational devices by the FDA and, thus, could not be sold at a profit in the United States, information on U.S. sales is not readily available. However, using the number of clinical placements as a proxy for sales, the industry appears to be concentrated among four firms that account for 79 percent of worldwide placements and 83 percent of placements in the United States (see table 7). As of August 1984, Technicare Corp. had placed more operational units in clinical settings (44) than any other manufacturer, garnering 30 percent of the 145 worldwide placements and 39

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[5] See app. C for information on specific manufacturers.

Table 7.—The NMR Imaging Device Industry: Market Share as Reflected in Clinical Placements[a]

	Current placements (as of August 1984)		Current market share[c]	
Company[b]	Worldwide	U.S. only	Worldwide	U.S. only
Technicare Corp.	44	36	30%	39%
Picker International	28	12	19	13
Diasonics Inc.	23	19	16	20
Siemens Medical Systems	19	10	13	11
Fonar Corp.	9	6	6	6
Philips Medical Systems	5	1	3	1
Bruker Instruments	4	2	3	2
Elscint Ltd.	4	2	3	2
General Electric Co.	4	3	3	3
M&D Technology Ltd.[d]	2	0	1	0
Nalorac Cryogenics	2	2	1	2
Toshiba Corp.[d]	1	0	1	0
Totals	145	93	100%	100%

[a] NMR imaging systems placed in clinical sites outside factory; human systems only (whole body and head).
[b] In descending order of worldwide market share, as of August 1984.
[c] Expressed as percentage of total current placements. Detail may not sum to 100 percent because of rounding.
[d] As of October 1983.

SOURCES: Interviews with manufacturers; Boteler, 1983 (20); American Hospital Association, 1983 (6); and "Imaging Equipment Sales Close In On $4 Billion Mark," *Diag. Imag.* 5(11):55-61, November 1983.

percent of those in the United States (36 of 93). Picker International was second, with 28 units worldwide (19 percent) and 12 in the United States (13 percent). Diasonics Inc. had placed 23 units worldwide (16 percent), with 19 of those in the United States (20 percent of the U.S. market). Siemens Medical Systems had slightly fewer placements, with 19 worldwide (13 percent) and 10 in the United States (11 percent).

NMR Imaging Systems. An important determinant of industry growth and seller concentration will be the product features offered in the NMR imaging systems. Manufacturers are investing great energy in product differentiation strategies designed to segment the market for NMR imaging devices (see discussion of nonprice competition policies of firms in the industry conduct section of this chapter). Considerable controversy exists over the optimal design and configuration of NMR imaging units (20). Much of the debate centers on magnet design (6), with various manufacturers pursuing different strategies.

At present, M&D Technology Ltd. is the only company that appears committed to resistive magnet design operating at relatively low field strengths (see table 8). At least five firms (Diasonics, Philips, Siemens, General Electric, and Nalorac Cryogenics) are strongly committed to superconducting magnet technology only. Philips and Siemens now offer both 5 and 15 kilogauss systems, whereas General Electric plans to market a 15 kilogauss model in 1984. Nalorac Cryogenics is developing three superconducting systems intended largely for research applications, with magnet strengths ranging from 10 to 40 kilogauss (see app. C).

Superconducting magnet systems are now offered by at least four other manufacturers, but three of them also offer resistive systems (Picker International, Technicare Corp., and Bruker Instruments) and one is experimenting actively with permanent magnets (Elscint Ltd.). Fonar Corp. is the only manufacturer that now bases its system design on permanent magnet technology, including a 3 kilogauss mobile, whole body unit. ADAC Laboratories is also developing a permanent magnet NMR imager and expects to have a production model ready in late 1985.

Buyer Concentration

Unlike the high seller concentration in the NMR imaging device industry, the number and diversity of potential buyers in the market is extraordinarily large, covering research laboratories and

Table 8.—Status of NMR Imaging Systems[a]

	NMR imaging system				
Company[b]	Magnet type	Field strength (kilogauss)	Bore size	Year first available	Clinical patients studied to date[c]
Bruker Instruments	R	1.3[d]	B	1979	100
	S	47	A	1979	
	S	19[d]	A or H	1982	
	R	2.4	B	1984	
CGR Medical Corp.	R	1.5	B	1982	0
	S	3.5	B	1983	
	S	5	B	1983	
Diasonics Inc.	S	5[d,e]	B	1981	NA
Elscint Ltd.	S	5	B	1982	NA
Fonar Corp.	P	0.4	B	1980	2,200
	P	3[d]	B	1983	
	P	3[d]	BM	1983	
General Electric Co.	R	1.2[f]	B	1982	600
	R	1.5[f]	B	1983	
	S	15[d]	B	1984	
M&D Technology Ltd.	R	0.4	B	197?	1,200
	R	0.8	B	1982	
Philips Medical Systems	R	1.5	B	1982	300
	S	30	A	1982	
	S	15[d]	B	1983	
	S	5[d]	B	1983	
Picker International	R	1.5[d]	B	1978	NA
	S	3	B	1981	
	S	5[d]	B	1983	
Siemens Medical Systems	R	1.2	B	1980	800
	R	2	B	1981	
	S	5[d]	B	1983	
	S	15[d]	B	1983	
Technicare Corp.	S	15[d]	A	1980	4,750
	R	1.5[d]	H	1981	
	S	3[f]	B	1982	
	S	5[d]	B	1983	
	S	6	B	1983	
	S	15	B	1983	
Toshiba Corp.	R	1.5	B	NA	NA

NA = Not available.

KEY: Magnet type: P = Permanent
R = Resistive
S = Superconducting
Bore size: A = Animal
B = Whole body
BM = Whole body (mobile)
H = Head

[a] As of August 1984.
[b] In alphabetical order.
[c] As of October 1983.
[d] Probable commercial prototype system(s).
[e] System operating at 3.5 kilogauss.
[f] No longer available.

SOURCES: Interviews with manufacturers; Boteler, 1983 (20); and American Hospital Association, 1983 (6).

various types of clinical facilities. Likely buyers in the clinical segment of the market include hospitals, private radiology groups, and health maintenance organizations (HMOs). Many manufacturers are optimistic that more than half of the 5,900 non-Federal, short-term general hospitals in the United States (5) will purchase NMR imagers by 1990. The prime buyers will be the leading teaching hospitals and medical centers, followed by large urban and moderate-sized community hospitals with bed capacities of at least 200. In the United States alone there are over

1,700 hospitals meeting this description (5) and a large number in Canada and Western Europe. NMR imaging manufacturers also expect to make in-roads into other segments of the U.S. hospital industry, including the smaller independent community hospitals (100 to 199 beds); Federal Government hospitals in the Veterans Administration, Department of Defense, and Public Health Service systems (numbering around 350 facilities); and long-term and specialty hospitals (roughly 1,000). Hospital chains, particularly investor-owned corporations, are expected to be prime purchasers of NMR imagers (see the discussion of hospital strategies in ch. 5).

Several hundred NMR imaging units are expected to be sold worldwide to private radiology groups and to physicians' offices outside hospitals. The approximately 236 HMOs and prepaid health plans in the United States (193) are another potential source of buyers, with some likely to purchase multiple units for outpatient as well as inpatient settings.

Finally, the medical research community is viewed as an important market segment. At least two manufacturers (Nalorac Cryogenics and JEOL) are firmly committed to developing NMR imaging systems specifically intended for research applications. Both firms are investing in superconducting magnet systems that will operate at relatively high field strengths and be capable of performing phosphorus spectroscopy as well as proton NMR imaging.

Barriers to Entry

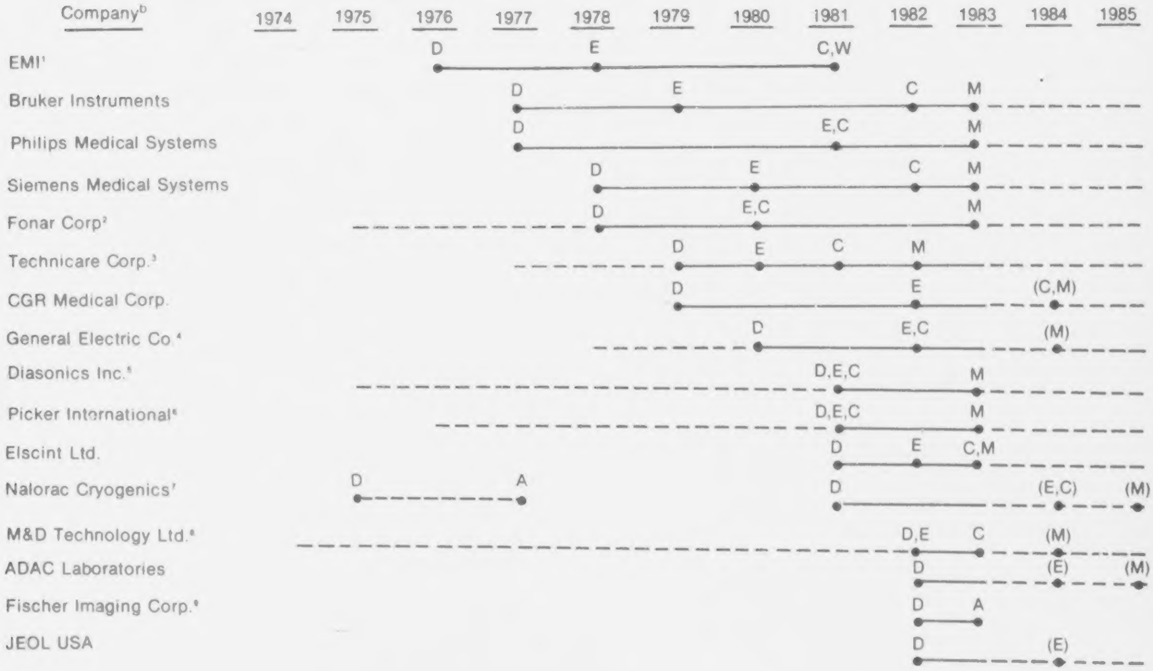
The ability of relatively small firms to enter the NMR imaging device industry depends on several key factors: their ability to attract adequate capitalization and technical/scientific talent for R&D, the development of strong university ties for collaborative research, and the ability to market products once they have been developed. At present, three small, single-product firms comprise 16 percent of the total number of firms in the industry (3 of 19 firms). Among them, one (Fonar Corp.) has attained advanced R&D status, and a second (M&D Technology Ltd.) stands on the threshold of commercial production. In order to understand the importance of these achievements, it is necessary first to examine the chronological development of the NMR imaging device industry.

Industry Development. The birth of the NMR imaging device industry can be traced to 1976 when EMI began work on building an NMR imaging machine. In 1977, two other companies (Bruker Instruments and Philips Medical Systems) embarked on parallel courses of NMR imaging R&D (see fig. 10). Between 1978 and 1980, five additional firms entered the industry. Fonar, drawing on several years of research by Raymond Damadian, was the first American company (and the only small single-product firm) to make a firm financial commitment to NMR imaging R&D during this period. Since 1980, the industry has experienced rapid growth, with four new entries in 1981 and another four in 1982. Data for the Japanese NMR imaging device industry are incomplete, but it is believed that several Japanese companies also entered the market during this time.

The pattern of NMR imaging development, i.e., the sequence of steps through which a manufacturer must pass in order to reach full production capability, generally consists of four major steps (see fig. 10):

1. *Corporate decision*—the manufacturer makes a corporate decision to invest in R&D activities and marshals its resources (capital, staff, facilities, materials) to assemble a program development effort whose first objective is to produce an experimental prototype or engineering model.
2. *Experimental prototype*—upon attaining this goal, the manufacturer can begin in-house testing that proceeds through several stages using "phantom" (inanimate) objects at first, and then laboratory animals and humans as imaging subjects. The knowledge and experience gained in the process facilitate the refinement of both system hardware and imaging techniques.
3. *Clinical placement outside the company plant*—manufacturers differ somewhat in their approach to clinical testing. Some prefer initial testing with humans on experimental in-house systems before seeking outside clinical placements of investigational units. Others choose to perform all clinical

Figure 10.—Chronological Development of the NMR Imaging Device Industry[a]



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[a] Information on chronology of events not available for Ansoldo SPA, Hitachi Ltd., Instrumentarium Oy, OMR Technology (now Xonics), Sanyo Electric, Shimadzu Corp., and Toshiba Corp.

[b] In order of market entry based on corporate decision to invest in NMR imaging.

KEY: D = Corporate decision to invest in R&D efforts for NMR imaging
E = First experimental prototype/engineering model available
C = First clinical placement of an NMR imaging unit outside the company's plant
M = First commercial/marketing prototype system available for placement
A = Acquisition of company by other firm
W = Withdrawal of company from the industry
Letter symbols in parentheses ( ) indicate projected events in the future
Dotted lines to the left of decision (D) points reflect R&D work that preceded formal company involvement or formation

[1] Began NMR R&D in 1976; produced first engineering model in 1978; sold its NMR imaging technology to Picker International in October 1981.

[2] Founded in 1978 as RAANEX Corp.; became Fonar Corp. in 1980.

[3] Parent company, Johnson & Johnson, made initial commitment as early as 1977, but major R&D effort did not begin until the acquisition of Technicare in 1979.

[4] Early R&D work in phosphorus spectroscopy began in 1978, but firm corporate commitment to NMR imaging was not made until 1980.

[5] Initial R&D bagan as a University of California, San Francisco (UCSF) project with outside funding. In 1976, the Pfizer Corp. began funding the work. In 1981, Diasonics Inc. purchased the rights to all patentable NMR technology developed under the UCSF-Pfizer agreement.

[6] Formed in April 1981 after GEC of England acquired the Picker Corp. and merged it with GEC Medical and Cambridge Medical Instruments. GEC of England had begun NMR imaging R&D in 1977. In October 1981, Picker International purchased all NMR imaging technology that had been developed independently by EMI of England since 1976.

[7] Began early R&D on superconducting NMR systems in 1976. In 1977, the company was acquired by Nicolet Instruments Corp. In 1981, the original founder of Nalorac Cryogenics purchased the company back from Nicolet and reaffirmed its commitment to developing NMR imaging systems.

[8] Formed in 1982 to commercially develop the NMR imaging system that had evolved from the work of Professor Mallard at Aberdeen, Scotland since 1974.

SOURCE: Interviews with manufacturers.

testing in outside clinical facilities with whom they have established close collaborative relationships. Regardless of the strategy employed, clinical placement of investigational systems outside the company's plant is a major step toward obtaining critical data for further refinement of the product and for defining the optimal configuration of the commercial system to be produced.

4. *Commercial prototype*—this is the last step of advanced R&D prior to full commercial production. The design and development of this prototype or commercial model often occurs concurrently with intensive clinical testing. Some manufacturers have cautiously delayed commercial prototype development until *after* thorough clinical testing in order to specify the best commercial design possible.

In the case of NMR imaging R&D, the time span required for completion of all four steps appears to have decreased over the years (see fig. 10). The early firms entering the market (e.g., EMI, Bruker Instruments, Philips Medical Systems, Siemens Medical Systems, and Fonar Corp.) each took 2 to 4 years to produce their first experimental systems. By contrast, firms entering the market in the last 2 to 3 years either have attained, or plan to attain, this goal in significantly less time. Overall, the actual or projected time frames of these late participants in NMR imaging are very much compressed, owing to the strong pressures of competition and to the knowledge about NMR imaging design conferred upon them by the pioneering efforts of their predecessors.

The pathways for entry[6] into the market have varied by manufacturer (see fig. 10). Essentially, four different routes have been followed, some simultaneously:

- *Government-supported R&D*—EMI entered the NMR market in 1976 with grant support from the Department of Health and Social Security (DHSS) in Great Britain. British Government support of university-based R&D at Nottingham and Aberdeen during the 1970s also later benefited Picker International and M&D Technology Ltd., respectively, when they decided to enter the NMR imaging market. Three firms (Bruker, Philips, and Siemens) have received grants from the West German Government, but only after each had initiated NMR program development with company resources.
- *University-based R&D*--all four small, single-product firms emerged as a direct result of university-based R&D at the following institutions: State University of New York (Fonar Corp.); University of Aberdeen (M&D Technology Ltd.); University of Nottingham (Nalorac Cryogenics); and University of California, Los Angeles (OMR Technology). In the case of Nalorac Cryogenics, the company's founder, James Carolan, had worked at Nottingham and later at Bruker before establishing his own firm.
- *Acquired technology*—two firms have successfully employed this strategy to accelerate their market entry and their progress toward advanced R&D. Picker International in 1981 purchased all NMR imaging technology that had been developed by EMI of England since 1976. That same year, Diasonics Inc. purchased the rights to all patentable NMR technology developed by Pfizer under an agreement with the University of California, San Francisco. A third firm, Fischer Imaging Corp., also sought to purchase NMR imaging technology from other manufacturers, but eventually was acquired by Diasonics Inc. in May 1983.
- *Internally based R&D*—the remaining firms in the industry have generally relied on internal R&D operations to develop their own NMR imaging technology. General Electric, Philips, Siemens and Technicare are examples of large companies marshaling their considerable R&D resources for directed NMR program development. Elscint and ADAC Laboratories have also committed themselves to internal R&D without benefit of government funding or of "off-the-shelf" technology. At least three firms (Bruker, Philips, and JEOL) have been able to draw directly on their corporate experience in manufacturing research laboratory NMR spectrometers.

The major elements affecting a company's ability to enter the marketplace generally have included the availability of capital, staff expertise, corporate experience, and collaborative links with major university research groups.

Capital Requirements for Market Entry. Interviews with manufacturers suggest that capital requirements for R&D have not been unduly excessive for those who have entered the field. Industry sources estimate that a new firm, or a firm lacking prior experience in NMR spectroscopy, requires between $4 million and $15 million for *initial* capitalization of R&D. This estimate does not include the capital required for expanding production capacity or for vertical integration of NMR imaging-related products, e.g., the capacity to build one's own magnets.

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[6] The paths for entry do not necessarily reflect subsequent R&D strategy and are not mutually exclusive.

Table 9 shows the R&D expenditures incurred up to October 1983 by 12 companies involved in NMR program development. Expenditure levels are reflections, in part, of a company's stage of R&D effort. For instance, the four firms reporting expenditures of $1 million to $5 million have only recently entered the market and are engaged in *early* R&D. By contrast, the six companies reporting expenditures in excess of $10 million are involved in *intermediate* (two firms) or *advanced* (four) stages of R&D. There are exceptions to this pattern: the two firms with expenditures in the $6 million to $10 million range have both attained *advanced* R&D status.

Staff Requirements for Market Entry. The importance of staff expertise to R&D activities in NMR imaging cannot be overstated. As mentioned earlier, Fonar Corp. and M&D Technology Ltd. were formed around innovative scientists and their specific techniques or methodologies. The technical complexity of NMR imaging dictates that manufacturers assemble R&D teams with expertise in such fields as physics, chemistry, engineering, and computer science. Specific knowledge of NMR spectroscopy is valuable. Several firms, including Technicare, Picker International, and General Electric, have aggressively recruited individuals who conducted some of the earliest NMR research in England in order to augment their in-house R&D staff talent.

For small firms, staff recruitment and development may be a constraint. A "critical mass" of at least five to six scientists appears to be necessary before a company can actively initiate R&D. Continued staff growth, as R&D activities mature, is vital to company survival. In the face of tight resource constraints, some firms have had to augment in-house expertise with outside consultants. Equally important for sustained program development is the need to establish a top-notch marketing and sales force. The larger, well-established firms with existing sales networks hold a critical competitive edge over smaller companies that lack such organization and expertise. Marketing and sales acumen may prove to be a decisive factor in the competitive marketplace that is rapidly developing.

Table 9.—Research and Development Expenditures Among Firms in the NMR Imaging Device Industry

R&D expenditures to date[a]	Number of firms reporting	Percentage
<$5 million	4	33%
$6-10 million	2	17
$11-20 million	1	8
>$20 million	5	42
Total	12	100%

[a] As of October 1983.

SOURCE: Interviews with manufacturers.

Collaborative Research With Universities and Major Medical Centers. University or major medical center research ties are considered essential in the industry. Every manufacturer engaged in either intermediate or advanced stage R&D in October 1983 had a close collaborative relationship with one or more universities or major medical centers (see table 10). The lack of university research links early in R&D is not necessarily a barrier to market entry for small firms, but future company survival—particularly in the clinical phases of product testing—may depend on the nature and quality of such agreements. Large firms also recognize the importance of collaborative research. Technicare, for example, has a stated policy of not placing units in clinical sites unless close working arrangements with the institutions can be established. Acquisition of clinical data is extremely important to the manufacturer in preparing for FDA premarket approval and for coverage decisions by third-party payers in the health care system.

Patents. Among the Federal policies that have been developed to promote innovative research and product development are those related to the protection of discoveries by patents. Although a thorough discussion of patent law and its commercial and societal ramifications is beyond the scope of this report (and the expertise of its authors), a few comments can be made regarding the NMR-related patents and their impacts.

A number of components of NMR imaging and spectroscopy systems would seem patentable. Among these are designs of: 1) the magnet used to produce the static magnetic field; 2) the radiofrequency coils used to emit and receive radiofrequency waves; 3) the gradient coils used to permit spatial encoding; and 4) the software techniques

Table 10.—Manufacturers' Collaborative Arrangements With Universities/Medical Centers[a]

Company:[b]	university/medical center
ADAC Laboratories:	Negotiated, yet to be announced.
Bruker Instruments:	Baylor College of Medicine, Houston, TX
	Yale University, New Haven, CT
CGR Medical Corp.:	None in USA (number in Europe not available)
Diasonics Inc.:	University of California, San Francisco (UCSF)
	University of Texas, Dallas
	University of Michigan, Ann Arbor
Elscint Ltd.:	Hebrew University, Jerusalem, Israel
	Weitzman Institute, Rehovoth, Israel
Fonar Corp.:	University of California, Los Angeles (UCLA)
General Electric Co.:	Medical College of Wisconsin, Milwaukee
	University of Pennsylvania, Philadelphia
	Yale University, New Haven, CT
	Duke University, Durham, NC
JEOL USA:	None at present
M&D Technology Ltd.:	University of Aberdeen, Scotland, U.K.
Nalorac Cryogenics:	None at present
Philips Medical Systems:	Neurological Institute, Columbia-Presbyterian Hospital, New York
	University of Leiden, The Netherlands
Picker International:	University of Nottingham, Nottingham, U.K.
	Royal Postgraduate Medical School and Hammersmith Hospital, London, U.K.
	Mount Sinai Hospital, Cleveland, OH
	Mayo Clinic, Rochester, MN
	Bowman Gray Medical School, Winston-Salem, NC
	University of British Columbia, Vancouver, Canada
	City of Faith Medical and Research Center, Tulsa, OK
	National Institutes of Health, Bethesda, MD
	University of Iowa, Iowa City
	Queens Square Hospital, London, U.K.
Siemens Medical Systems:	Washington University, St. Louis, MO
	University of Hanover Medical Center, Hanover, West Germany
	Radiological Institute, Frankfurt, West Germany
	Radiological Institute, Munich, West Germany
	Mount Sinai Medical Center, Miami, FL
	Allegheny General Hospital, Pittsburgh, PA
Technicare Corp.:	Massachusetts General Hospital, Boston, MA
	University Hospital, Cleveland, OH
	Cleveland Clinic Foundation, Cleveland, OH
	University of Kentucky, Lexington
	Indiana University, Indianapolis
	Hershey Medical Center, Hershey, PA
	Millard Fillmore Hospital, Buffalo, NY
	St. Joseph's Hospital, London, Ontario, Canada
	Johns Hopkins University, Baltimore, MD
	Ontario Cancer Institute, Toronto, Canada
	Charlotte Memorial Hospital, Charlotte, NC
	New York Hospital, New York
	Vanderbilt University, Nashville, TN
	Defalque Clinic, Charleroi, Belgium
	University of Florida, Gainesville
	Baylor University Medical Center, Dallas, TX
	Rush Presbyterian-St. Luke's Medical Center, Chicago
Toshiba Corp.:	Toshiba General Hospital, University of Tokyo, Japan

[a]As of August 1984, except M&D Technology Ltd. and Toshiba Corp. are as of October 1983. Information not available for Hitachi Ltd., OMR Technology (now Xonics Inc.), Sanyo Electric, and Shimadzu Corp.
[b]In alphabetical order.

SOURCES: Interviews with manufacturers and American Hospital Association, 1983 (6).

used for spatial encoding, data gathering and image reconstruction.

Neither Lauterbur nor SUNY-Stony Brook patented Lauterbur's originial NMR imaging technique or the apparatus (115).[7] On March 17, 1972, however, Raymond Damadian filed a patent application for an "Apparatus and Method for Detecting Cancer in Tissue" and received a patent in February 1974. Damadian has apparently filed an additional patent application in the United States, as well as patent applications in foreign countries (65). A number of NMR-related patents are apparently also held in a patent portfolio by the British Technology Group, formerly the National Research Development Corp. (120). Information regarding the types of license agreements, if any, related to such patents is not available. No attempt has been made to gather comprehensive information for this report regarding the number and types of patents held by NMR manufacturers.

A primary concern regarding patents is that they might create undesirable barriers to the entry of potential NMR manufacturing competitors into the marketplace. However, the existence of at least 19 manufacturers of NMR imaging systems suggests that patents have not created such a barrier; the manufacturers we interviewed concurred with this view. Whether patentable discoveries will emerge, prohibitively expensive cross-licensing agreements will be devised, or pending lawsuits[8] will be settled in such a way as to change this situation is difficult to predict.

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[7] Apparently, the SUNY-Stony Brook was advised by an outside consultant not to proceed with a patent application.

A second policy concern regarding patents is that manufacturers might: 1) stifle the prompt dissemination of scientific discoveries made by those university-based researchers whom they support in order to provide time for filing patents or 2) redirect the focus of university-based research away from "basic science" and toward the development of patentable devices and techniques. The existence of a large number of industry-university collaborative NMR research relationships (see table 10) suggests that universities have not found such research agreements prohibitively restrictive.[9]

This empirical inference was confirmed by discussions with a number of investigators whose NMR research is being supported in part by industry (1,184). Others, however, voiced concern that the scope of their research was more constrained when sponsored by industry than by NIH. Such a concern would seem to be more an argument for Federal research funds than an indictment of patents.

Finally, it is difficult to determine how beneficial the protection afforded by patents has been to the commercial development of NMR in this country. It is possible, for example, that many manufacturers have relied more on maintaining discoveries as "trade-secrets," rather than revealing confidential information in patent applications. Of interest in this regard, however, is the belief voiced by Lauterbur that acquisition of a patent by either SUNY-Stony Brook or himself would have accelerated commercial development of NMR imaging devices in the United States by virtue of providing a means of protecting a manufacturer's competitive advantage (116).

Regulatory Policies. We surveyed NMR manufacturers about their perceptions of the impact of various regulatory policies on the placement of their products in clinical sites.[10]

Of the various Federal and State policies affecting technological development and diffusion, none was perceived by manufacturers to be a serious constraint on NMR *development*. The FDA premarket approval (PMA) process is generally regarded as a time-consuming "hurdle" that is not overly obstructive. None of the firms interviewed felt that the PMA process had influenced either the pace of R&D activities or the placement of investigational units at clinical sites. (For a more complete discussion of issues pertaining to the FDA and its PMA process, see ch. 7.)

By contrast, third-party payment policies, and to a lesser degree, State certificate-of-need programs, appear to cause major concern among manufacturers as potential barriers to NMR *diffusion*. Coverage policy decisions of the Federal Medicare program, State Medicaid agencies, local Blue Cross/Blue Shield plans, and commercial insurance companies are considered critical to the future marketing of NMR imaging devices. Unfavorable coverage decisions—or even moderate delays in decision making—by the Health Care Financing Administration (HCFA) and other third-party payers could pose serious financial problems for those manufacturers in advanced stages of R&D. Coverage denials for NMR imaging could conceivably destroy the hospital segment of the market and militate strongly against entry of new firms into the industry. State prospective payment programs are viewed by manufacturers with considerably less trepidation since, under many such programs (e.g., Maryland, New York, Massachusetts), hospitals have retained wide discretion in their capital-equipment purchases.

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[8] On Sept. 20, 1982, Fonar Corp. and Dr. Raymond Damadian filed suit in the U.S. District Court in Massachusetts against Johnson & Johnson and its subsidiary, Technicare Corp. (65). The suit charges Johnson & Johnson and Technicare with willfully infringing on Damadian's patent for using Nuclear Magnetic Resonance in detecting and diagnosing human disease and with unfair competition and interference in Fonar's ability to successfully market the apparatus covered by the patent. The defendants have denied the allegations and requested a judgment declaring the patent invalid. The matter is in the discovery stage (65).

[9] Many research agreements between industry and academia enable universities to benefit financially from the discoveries made by their faculty. Diasonics Inc., for example, holds the exclusive right to obtain an exclusive license to all patentable NMR technology discovered pursuant to the research project it supports at the University of California. Under the terms of the license, the university is entitled to a royalty of 0.56 percent of the selling price of any NMR system sold by Diasonics that includes technology patented by the university (51).

[10] The views expressed by the manufacturers should not be considered to represent the views of either the authors or OTA.

State certificate-of-need (CON) programs, on the other hand, are perceived as potentially troublesome constraints that might delay—or even limit—the placement of NMR imaging devices in specified geographic areas. Some manufacturers feel that CON policies could prove unusually restrictive in some areas of the country despite favorable coverage decisions by third-party payers. Should this occur, NMR diffusion could slow noticeably in the United States, sending discouraging signals to firms contemplating market entry.

Diversification of Firms

The firms that constitute the NMR imaging device industry display considerable diversity in their product lines and operations. Twelve companies (63 percent) manufacture nonhealth care related products either directly or through a parent firm (see table 11). These products range from assorted electrical equipment and household appliances to electron microscopes and instruments for testing. In many instances, sales of these products far exceed those of health care related equipment and products.

Of the 15 firms identified in table 11 as multiproduct entities, all but two (Bruker Instruments and JEOL) produce diagnostic imaging equipment *other* than NMR imaging. Of these, six (CGR, Elscint, General Electric, Philips,[11] Picker, and Siemens) offer full diagnostic imaging product-lines, including CT, ultrasound, nuclear medicine, digital radiography, and conventional X-ray and fluoroscopy. An additional four firms (ADAC Laboratories, Hitachi, Technicare, and Toshiba) manufacture products in three or more diagnostic imaging modalities.

The diverse nature of industry firms serves to benefit their R&D efforts in NMR imaging by:

- offering technical expertise gained in the development and marketing of other diagnostic imaging modalities, such as CT and nuclear medicine;
- accelerating product development based on corporate experience with related technologies in nonhealth care fields, such as NMR spectroscopy; and
- increasing the R&D resource base available to NMR imaging development through the sales of various other products in both health care and nonhealth care fields.

Diversification in the industry is likely to increase in the future, as some small firms expand operations into new product lines and as some large companies augment their already diverse portfolios.

Acquisition and Merger Activity

Since its inception in the mid-1970s, the NMR imaging device industry has witnessed a considerable number of acquisitions, mergers, and important trade agreements among its member firms. Acquisition and merger activity may be classified into four major groups (9,31,139):

- *Product extension*—in which a company gains entry into a related market by acquiring a firm that sells products not presently produced by the parent.
- *Market extension*—in which a company consolidates or increases its market share by acquiring a firm in the same product line.
- *Conglomerate merger*—in which a parent company acquires another company that is unrelated in either product or market.
- *Vertical integration*—in which a company acquires another firm whose activity is important to the processing, manufacturing, sale, or distribution of the parent company's product.

Most acquisitions and mergers in the industry have been oriented toward product extension involving various diagnostic imaging modalities (see table 12). Among these have been two cases involving NMR imaging. In one instance, Diasonics Inc., acquired the rights to NMR imaging technology developed under an agreement between Pfizer, Inc. and the University of California, San Francisco (UCSF) Radiological Imaging Labora-

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[11] Philips manufactures nuclear cameras, sold in the United States through ADAC Laboratories.

Table 11.—Diversification Among Firms in the NMR Imaging Device Industry[a]

	Health-care-related products						
	Diagnostic imaging[b]						
Company	CT	US	NM	DR	XR	Other medical products	Non-health-care-related products
ADAC Laboratories			✓	✓	✓	Radiation therapy planning; special procedures room; clinical information systems; medical linear accelerators	Instruments for non-destructive testing
Bruker Medical Instruments			NMR only			ECG monitors[c]; mobile defibrillators[c]; patient monitoring systems[c]	NMR spectrometers
CGR Medical Corp.	✓	✓	✓	✓	✓	None	Assorted electrical appliances and equipment[c]
Diasonics Inc.[d]		✓				None	None
Elscint Ltd.	✓	✓	✓	✓	✓	None	None
Fonar Corp.			NMR only			None	None
General Electric Co.	✓	✓	✓	✓	✓	Assorted electromedical equipment	Assorted electrical appliances and equipment
Hitachi Ltd.	✓	✓		NA	✓	NA	Assorted electrical appliances and equipment
JEOL USA			NMR only			Radioimmunoassay equipment; blood gas analyzers; fluid analyzers	NMR spectrometers; electron microscopes[c]
M&D Technology Ltd.			NMR only			None	None
Nalorac Cryogenics			NMR only			None	Superconducting high-resolution analytical NMR magnets, gradient coils, power supplies, dewars, NMR probeheads
OMR Technology			NMR only			None	None
Philips Medical Systems[e]	✓	✓	✓	✓	✓	Surgical supplies;[c] dental equipment;[c] assorted electromedical equipment	NMR spectrometers; assorted electrical appliances and equipment[c]
Picker International	✓	✓	✓	✓	✓	ECG equipment; other electromedical equipment[c]	None
Shimadzu Corp.		✓		NA	✓	Assorted electromedical equipment	Assorted products and equipment
Siemens Medical Systems	✓	✓	✓	✓	✓	Assorted electromedical equipment	Assorted electrical appliances and equipment
Technicare Corp.	✓	✓	✓	✓		Surgical instruments and supplies;[c] dental equipment	None
Toshiba Corp.	✓	✓		✓	✓	NA	Assorted electrical appliances and equipment

NA = Information is either unavailable or unknown.

[a] Firms listed in alphabetical order. No data for Sanyo Electric, which is recognized for its assorted non-health-care-related products. Information is as of August 1984, except for Hitachi Ltd., M&D Technology Ltd., OMR Technology, Shimadzu Corp., and Toshiba Corp., all of which are as of October 1983.

[b] Diagnostic imaging modalities *other* than NMR imaging.

[c] Products made by parent firm only (see table 6 for information on parent companies).

[d] Diasonics also manufactures surgical C-arm imaging equipment.

[e] Philips designs and manufactures nuclear cameras, sold in the United States through ADAC Laboratories.

Key for diagnostic imaging: CT = computed tomography; US = ultrasonography; NM = nuclear medicine; DR = digital radiography; XR = conventional X-ray and fluoroscopy.

SOURCE: Interviews with manufacturers; Arthur Young & Co., 1981 (9); Boteler, 1983 (20); and Emmitt & Lasersohn, 1983 (60).

tory. In the other, Fischer Imaging Corp. entered into an agreement (*not* a merger) with M&D Technology Ltd. to become the exclusive marketing agent for M&D's NMR imager. This agreement was soon terminated, however, when Fischer was acquired by Diasonics in a product extension merger whose prime target was Fischer's line of X-ray equipment.

Market extension mergers have occurred less frequently in the young industry, but one case involving NMR imaging stands out: Picker International's acquisition of the technology developed by EMI of England. In this instance, Picker sought to reinforce and complement the NMR imaging technology previously developed independently by its parent firm, GEC of England. As with

Table 12.—Acquisitions, Mergers, and Key Trade Agreements in the NMR Imaging Device Industry Since 1971

Year and nature of acquisition/merger/trade agreement activity	Comment
ADAC Laboratories:	
1981: Agreement with Picker International for manufacturing digital angiography systems	—
1982: Agreement with Fischer Imaging Corp. for manufacturing digital angiography systems	Agreement terminated same year
Bruker Instruments:	
1982: 25% of company ownership acquired by IBM	IBM provides grant support to MIT and Harvard for NMR imaging research at Brigham & Women's Hospital (Boston) using Bruker equipment
1983: Acquired Oxford Research Systems from Oxford Instruments	—
CGR Medial Corp.:	
1971: Created by the acquisition of Westinghouse Medical X-Ray Division by CGR of France	Market extension: X-ray equipment
1979: CGR of France merged with Thompson-CSF to form Thompson-Brandt	Conglomerate merger
Diasonics Inc.:	
1981: Acquired rights to NMR technology developed under agreement between Pfizer and the UCSF Radiological Imaging Laboratory	Product extension: NMR imaging
1981: Acquired rights to cardiology ultrasound technology developed by Varian Associates	Product/market extension: phased array ultrasound
1982: Acquired Sonotron Holding A.G.	Vertical integration: Western European distributorship
1983: Acquired Sonics Imaging, Inc.	Vertical integration: Southeastern U.S. distributorship
1983: Acquired Fischer Imaging Corp.	Product extension: X-ray equipment[a]
Fischer Imaging Corp.:	
1980: Acquired the Medical Ultrasound Division of EMI	Product extention: ultrasound
1982: Agreement with ADAC Laboratories (see above)	(See ADAC Laboratories above)
1983: Agreement with M&D Technology Ltd. to become exclusive marketing agent for M&D NMR imager	Product extension: NMR imaging[b]; agreement terminated same year following acquisition by Diasonics (NMR) Ltd.
1983: Acquired by Diasonics Inc.	(See Diasonics Inc. above)
General Electric:	
1980: Acquired Thorn (CT Scanning Division of EMI)	Market extension: CT scanning
JEOL USA:	
1973: Parent firm, JEOL of Japan, acquired by Mitsubishi	Conglomerate merger: NMR spectroscopy[c]
1982: Agreement with Smith, Kline & French Laboratories for joint research into NMR spectroscopy	—
M&D Technology Ltd.:	
1982: Formed and financed by a combination of private and public investors	—
1983: Agreement with Fischer Imaging Corp. (see above)	(See Fischer Imaging Corp. above)
Nalorac Cryogenics:	
1977: Acquired by Nicolet Instruments	Product extension: superconducting magnets
1982: Divested by Nicolet Instruments and reestablished as independent firm	
Picker International:	
1981: Created by the acquisition of the Picker Corp. by GEC of England, and its subsequent merger with GEC Medical and Cambridge Medical Instruments	Product extension: X-ray equipment, CT scanning
1981: Acquired rights to NMR technology developed by EMI	Market extention: NMR imaging
1981: Agreement with ADAC Laboratories (see above)	(See ADAC Laboratories above)
Technicare Corp.:	
1979 Acquired by Johnson & Johnson, Inc., from Ohio Nuclear	Product extension: CT scanning
1982: Acquired Magnet Corp. of America	Vertical integration: superconducting magnets

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[a] Diasonics' prime purpose in acquiring Fischer Imaging Corp. was to obtain radiographic and fluoroscopic equipment to which it could add its computer software. Fischer Imaging Corp. had, by May 1983, already made a commitment to NMR imaging, but had not yet begun extensive R&D.

[b] Fischer's May 1983 marketing agreement with M&D Technology Ltd. was an attempt to extend its product line into NMR imaging without having to conduct extensive R&D efforts. Two weeks after signing the agreement, Fischer was acquired by Diasonics.

[c] JEOL of Japan nad been manufacturing NMR spectrometers since 1960. Following its acquisition by Mitsubishi, R&D efforts continued but it was not until 1982 that the company formally entered the NMR imaging field.

[d] Johnson & Johnson had developed interest in NMR imaging as early as 1977, but it was not until after the acquisition of Technicare (and its CT technology) that serious R&D efforts into NMR imaging were undertaken.

SOURCES: Interviews with manufacturers; Arthur Young & Co., 1981 (9); and Emmitt & Lasersohn, 1983 (60).

Diasonics' acquisition of the Pfizer-UCSF technology, Picker used its new technology to accelerate its market entry and to catapult to the industry forefront.

At least three mergers in the industry have involved vertical integration. In one case, integration has been "backward": Technicare's purchase of Magnet Corp. of America for the purpose of building its own superconducting magnet systems (see subsequent discussion in this chapter of the magnet manufacturing industry). The other two mergers represent "forward" integration whereby Diasonics acquired companies to expand its sales and distributorship network to specific geographic areas (see table 12 and later discussion in this chapter of vertical integration under "industry conduct").

Trade agreements involving marketing and distribution rights are fairly common in the industry, and those listed in table 12 are probably but a subset of all transactions that have taken place. Joint research ventures among firms, on the other hand, are rare, if not nonexistent. Manufacturers tend to be secretive about their NMR imaging designs and place units in clinical settings only if the hospitals agree *not* to accept a companion unit from a competitor for comparative study purposes.

As the NMR imaging device industry matures, one may expect further market extension and product extension mergers as some smaller firms are acquired by larger competitors or by firms seeking to enter the industry.[12] A high degree of vertical integration is also likely, as many firms will seek to expand internal capacity for marketing and distribution of products and for production of NMR component parts (e.g., magnets, cryogenic systems, and computer consoles and software). Magnet production capabilities are particularly important to manufacturers who wish to minimize both production costs and delays in receiving supplies in order to stay competitive with other companies. In addition to Technicare, which owns a magnet company, at least five other firms (Bruker, Diasonics, Elscint, Fonar, and Nalorac Cyogenics) possess in-house magnet manufacturing capabilities, while another seven plan to vertically integrate this function over the next 2 to 5 years.

The Magnet Manufacturing Industry. The magnet manufacturing industry is considerably more concentrated than the NMR imaging system manufacturing industry. Only a small number of firms make superconducting magnets, and little is known about manufacturers of resistive magnets.

According to a report from Hambrecht & Quist, as of September 1982 the majority of superconducting magnets used in NMR imaging systems worldwide had been supplied by a single manufacturer, Oxford Instruments, Ltd., a company based in the United Kingdom (80). For the year ended March 1983, Oxford Instruments had sales of 30 million English pounds, with profits of over 2.5 million pounds, an increase from 17.7 million pounds in sales and approximately 2 million pounds in profits in 1981-82 (119). In 1983, Oxford Instruments produced about six magnets per month and had secured long-term contracts to supply magnets to several NMR imaging manufacturers, including General Electric and Siemens (119). These orders would require an increase in Oxford's production capacity to about 12 magnets per month (119). To fulfill this increased demand, Oxford planned to hold a public stock offering in 1983 to secure funds to expand its production capability (119), ~~and~~ opened a manufacturing facility in the United States in a joint venture with Airco, Inc. (51). (Airco, a subsidiary of the British Oxygen Co. International, Ltd., has the capability of producing superconducting materials required in the manufacture of superconducting magnets.)

According to a 1982 prospectus issued by an American magnet manufacturer, Intermagnetics General Corp. (IGC), there are at least six American manufacturers selling superconducting magnets to NMR imaging manufacturers. To date, however, compared to Oxford Instruments, Ltd., these magnet manufacturers have not supplied significant numbers of superconducting magnets to NMR imaging manufacturers.[13]

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[12] The acquisition of OMR Technology by Xonics in late 1983 is a further example of product extension.

[13] IGC, for example, has been involved for over 10 years in the manufacture of the materials from which superconducting magnets are constructed. Recently, it has begun applying its expertise in superconducting technology to the development of superconducting

Two principal superconducting materials are commercially available for the construction of superconducting magnets: niobium - titanium (Nb-Ti) wire and niobium - tin (Nb_3Sn) tape. According to the 1982 IGC prospectus, there are several foreign manufacturers of Nb-Ti and Nb_3Sn. and IGC is the leading domestic producer of both materials (150). Airco, Inc.; Magnet Corp. of America (now a subsidiary of Technicare); and Supercon, Inc., are the other domestic suppliers of Nb-Ti and Nb_3Sn.

Oxford Instruments is the major supplier worldwide of resistive magnets for NMR imaging systems (80). Technicare and Bruker manufacture their own resistive magnets, and Fonar and OMR make their own permanent magnets.

With magnets accounting for an estimated 30 to 50 percent of the cost of NMR imaging systems,[14] it is not surprising that NMR imaging manufacturers are seeking to develop their own capacity to produce magnets. As stated previously, our survey of manufacturers found that six firms now produce at least some of their own magnets and seven others plan to develop their own capacity to manufacture magnets. According to IGC, however, it is unlikely that NMR imaging manufacturers will be able to meet their magnet supply needs themselves, and they are likely to want to have more than one source of magnets (154).

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magnets for use in NMR imaging systems. IGC increased its R&D expenditures from $264,000 in fiscal year 1981 to $1.5 million in fiscal year 1982 to help develop its magnet manufacturing capacity (104). It is currently manufacturing 0.5 tesla (T) and 1.5 T magnets. IGC supplied its first 1.5 T magnet (to Columbia-Presbyterian Medical Center) in March 1983 and planned to produce one to three magnets per month for the remainder of 1983. IGC has also begun construction of a new factory, which should be operational by 1984 and which will double its magnet production capacity. As of the end of August 1982, IGC had a backlog of $2.2 million in orders for superconducting magnets from NMR imaging manufacturers (105).

[14] According to M. J. Ross of IGC, 0.5 T magnets cost $300,000 to $350,000 and 1.5 T magnets cost over $500,000 (154).

INDUSTRY CONDUCT

The structural characteristics of the NMR imaging device industry (i.e., its high seller concentration, relatively easy market entry, considerable diversification, high degree of acquisition and merger activity, and low buyer concentration) have conflicting implications for competition among manufacturers. The behavior, or conduct, of the market is likely to be influenced not only by the policies and actions of individual firms, but also by their *reactions* to the policies of their rivals. Two important aspects of industry and market conduct are product pricing policies and nonprice competition strategies.

Product Pricing Policies

Based on interviews with manufacturers in 1983, the estimated sales price of a resistive magnet system is likely to range from $800,000 to $1.2 million. Superconducting magnet systems, depending on size and field strength, are expected to command prices between $1 million and $3 million, with the median expectation closer to $2 million. Since the FDA has only recently granted premarket approval for NMR imaging devices, there has been little experience with product pricing and sales.

Most of the manufacturers queried about sales price felt that it would not be a significant factor in determining future company market share. They instead stressed the importance of nonprice factors in differentiating their products from those of competitors (see discussion of product differentiation in this chapter). Only four firms viewed sales price as key to the coming competition for market share. Two companies expressly plan to segment the market on the basis of price, with lower magnet strength, less expensive NMR systems being offered to community hospitals and private radiology groups that may lack the requisite financial resources for purchasing the higher magnet strength, more costly models. One firm intends to develop medium-sized superconducting magnet systems that would sell for as low as $500,000 to $700,000. All four believe, though, that industrywide prices will decrease in the long-term (3 to 7 years from now) if for no other reason than that: 1) new magnet designs may lead to some efficiencies, 2) increased vertical integration in many companies should reduce production costs and create economies of scale, and 3) further experience with NMR imaging in clinical applications may point to an optimal system configuration that is less expensive to produce. It should be noted, however, that increased vertical integration could actually result in higher prices if such activity serves to diminish competition in the industry.

At least two manufacturers also believe that price cutting will not evolve simply as a consequence of the factors cited above, but rather become a conscious policy of the larger firms intent upon weakening and acquiring, or possibly driving out, smaller competitors. Such "predatory pricing" policies are employed in other industries (31). Their application here would, in the long run, make the NMR imaging device industry more concentrated than the current trend suggests (see earlier discussion of seller concentration and market share in this chapter). On the other hand, if one draws inferences from the experience with X-ray CT scanning, price competition may play little or no role in the coming industry "shakeout." Rather, as the next section suggests, nonprice factors may prove more important to company strategies.

Nonprice Competition

Product differentiation and vertical integration are both expected to figure prominently in the nonprice competition strategies of NMR imaging device firms. Given the diversity of potential buyers, the ability to differentiate one's product favorably from that of a rival may prove important to future company sales and market share. Vertical integration, in addition to its obvious economic benefits, may offer further advantage by raising barriers to entry for potential rivals (31).

Product Differentiation. Interviews with manufacturers have led to the identification and relative ranking, by tier, of nine *nonprice* factors considered important to NMR product differentiation in *future* sales efforts. In descending order of relative importance,[15] these elements are:

First Tier (4 factors):

1. *Image quality*—high-resolution images of various soft tissues in the head and body are considered essential to product sales. Almost without exception, this factor ranked first or among the top tier of elements.
2. *Product features and capabilities*—product features refer to the magnet type and field strength, bore size, radiofrequency coil design, computer system console and software, cryogenic systems for superconducting magnets, magnetic shields, etc. Product capabilities refer to measurement of T_1 and T_2 relaxation times, imaging capabilities, and spectral analysis capabilities in addition to proton NMR imaging. The relative importance of each feature or capability to a prospective buyer will depend on the buyer's fundamental imaging needs (e.g., clinical v. research) and level of sophistication. Innovative product capabilities, such as multislice imaging, are important means of product differentiation.
3. *Product reliability*—reliability is essential to the continuous operation of an imager and, therefore, is valued highly by prospective buyers. Lack of product reliability, such as the tendency for a magnet to "quench" (i.e., lose its magnetic properties), can have serious adverse effect on imager sales.
4. *Product service*—timely and responsive maintenance and repair service is important both for ensuring client satisfaction and for preserving company image. Distributor and service networks covering broad geographic areas are an important asset to marketing the product.

Second Tier (3 factors):

5. *Delivery time*—at present, delivery time can be very important to some buyers. Over time, however, as the industry matures and

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[15] The reader should bear in mind that these views are those expressed by NMR manufacturers, which may or may not coincide with the perceptions of potential buyers and users of the technology.

the production of NMR imaging units is streamlined in many firms, delivery time should become less important to buyers.

6. *Long-term viability of the manufacturer*—the larger, more well-established firms believe that size and tradition are important assets, and that buyers respond positively to companies whom they perceive to be viable for years to come. The smaller, newer firms concede this point, but argue that *product* characteristics (e.g., features and capabilities, image quality, reliability) will take precedence over company characteristics in determining future NMR imaging sales.
7. *Guarantee against technological obsolescence*—when purchasing expensive, new technologies, buyers frequently want assurance that the model they purchase today will not become obsolete in a short period of time. With a technology that is evolving and changing as rapidly as NMR imaging, such guarantees are difficult to make. Several manufacturers, therefore, have either: 1) delayed introduction of a commercial prototype until optimal system design can be satisfactorily determined, or 2) designed NMR systems that can be "upgraded" to accommodate new imaging needs or new advances in technology as they arise. However, when compared with other factors listed in the first tier, guarantees against product obsolescence were secondary in importance.

Third Tier (2 factors):

8. *Collaborative research*—at present, in the premarket stage of NMR imaging R&D, collaborative research with clinical centers holds great importance for manufacturers and hospitals alike. In the future, however, many firms expect that collaborative research will hold no more than tertiary importance (relative to the preceding factors) in influencing buyers'purchase decisions.
9. *Training and education*—a few firms believe that providing training services to buyers may become a distinguishing feature of some manufacturers' marketing and sales strategies. The relative importance of this factor to future sales, though, is not expected to be high.

Overall, product differentiation is emerging as an important part of each NMR manufacturer's nonprice competition strategy. Fonar Corp., for example, is placing great emphasis on its permanent magnet design. ADAC Laboratories, an acknowledged leader in "add-on" computer systems for diagnostic imaging modalities (185), intends to emphasize the company's strengths in image processing, data communication, and radiofrequency coil design as part of its marketing strategy, in addition to pursuing proprietary permanent magnet designs. General Electric has adopted a different tack, developing a 15 kilogauss superconducting magnet prototype, which the company believes will appeal to hospitals concerned about buying "adequate" magnet strength. Nalorac Cryogenics expects to differentiate its product by offering superconducting magnet systems that can operate within 10 to 20 kilogauss, but which can also be upgraded to 40 kilogauss for high-resolution animal studies and NMR spectroscopy. Regardless of the specific strategy employed, it seems clear that product differentiation will be important to each manufacturer's success and, in some cases, corporate survival.

Vertical Integration. In the earlier discussion of industry structure and corporate acquisition and merger activity, vertical integration in the NMR imaging device industry appeared to have important implications for production costs and, hence, for product pricing policies. Vertical integration can also be used by manufacturers to coerce rivals and influence market entry. For instance, in the NMR imaging device industry, the forward integration of distributorship networks could impede other firms from selling their products in some areas. Similarly, backward integration of magnet manufacturers could conceivably bar entry to potential competitors who are not capable of producing their own magnets and, therefore, must depend on outside suppliers.

Although at least one case of backward integration involving magnets has taken place in recent years (see Technicare in table 12), it is not likely that NMR manufacturers will gain control of either of the two major worldwide magnet suppliers (Oxford Instruments and Intermagnetics General Corp.). Instead, the net effect of many NMR manufacturers' plans to develop in-house magnet manufacturing capabilities will likely be to achieve greater independence from the magnet suppliers. An individual NMR imaging firm that chooses this strategy could gain a competitive edge only if its rivals did not vertically integrate in similar fashion, or, assuming that its rivals did follow suit, if its magnet operations were more efficient or produced higher quality magnets than those of its competitors. Vertical integration in the NMR imaging device industry, therefore, is more likely over the long run to influence industry conduct (i.e., product pricing and product differentiation) than industry structure (i.e., market entry by newcomers).

INDUSTRY PERFORMANCE

Industry performance is most frequently evaluated in terms of the efficiency and profitability of its firms (31). Common measures of *efficiency* include costs-to-sales ratios and percent of advertising or promotional costs-to-sales ratios (9). Data on advertising and sales in the NMR imaging device industry are nonexistent because the FDA prohibits promotion and profitmaking sales during the premarket approval stage of development. Thus, the relative efficiency with which various firms allocate their resources to build NMR imagers cannot be determined at this time. It is expected that, following FDA approval, promotional activities will abound in the industry, largely for product differentiation purposes.

Profitability has been measured as the rate of return on investment (or assets) or the price-cost margin (i.e., the gap between price and marginal cost). As with the previous case of measuring efficiency, FDA prohibition on making a profit from the placement of an investigational device has precluded the quantitative assessment of NMR industry profitability. Available data on the X-ray and electromedical industry show returns on *assets* ranging from 5.6 percent for the larger firms to 11.4 percent for companies with smaller assets (9). It is expected that NMR imaging sales will likely become an important source of company revenues for many manufacturers over the next few years (60).

THE FUTURE OF NMR IMAGING IN RELATION TO OTHER DIAGNOSTIC IMAGING MODALITIES

Given the uncertainties regarding the nature and impact of future health care regulations, as well as the extent to which the clinical potential of NMR imaging will be realized, it is difficult to make estimates of future sales of NMR imagers with any degree of certainty.

Table 13 provides data on estimated sales of various diagnostic imaging modalities projected by F. Eberstadt & Co., Inc. (60). As can be seen from the table, in mid-1983, worldwide sales of the diagnostic imaging industry were estimated at $4 billion per year, and this worldwide market is currently projected to continue expansion at a rate of 15 percent per year (60). Sales of ultrasound, digital X-ray equipment, and NMR imagers are expected to grow more rapidly than other segments of the diagnostic imaging market, primarily due to the reduction in or elimination of ionizing radiation associated with their use.

The table also shows that, despite a projected 21-percent increase in aggregate sales of X-ray modalities over the next 5 years, the percentage of all diagnostic imaging industry sales that can be attributed to X-ray modalities is expected to decrease by 41 percent (from a 72 percent to a 43 percent share) between 1983 and 1988. X-ray CT unit sales are projected to decrease during that time from $1 billion per year to $0.5 billion per year, a 76-percent decrease (from 25 percent down to 6 percent).

Table 13.—Diagnostic Imaging Industry Sales Growth Projections

	1983(E)		1988(E)		1983 to 1988		
Modality	Market size ($ millions)	Percentage of industry sales (%)	Market size ($ millions)	Percentage of industry sales (%)	Overall percentage change in market size (%)	Annual percentage change in market size (%)	Overall change in fraction of industry sales (%)
All X-ray modalities	$2,900	72.5%	$3,500	43%	+21%	+4%	−41%
Conventional X-ray	(1,300)	(32.5)	(500)	(6)	(−61)	(−17)	(−82)
Digital X-ray[a]	(600)	(15.0)	(2,500)	(30)	(+317)	(+33)	(+100)
CT	(1,000)	(25.0)	(500)	(6)	(−50)	(−13)	(−76)
Ultrasound	750	19.0	1,900	23	+153	+20	+21
Nuclear medicine	250	6.0	300	4	+20	+5	−33
NMR	100	2.5	2,500	30	+2,500	+90	+1,100
Total	4,000	100.0	8,200	100	+105	+15.0	—

[a] Includes both digital add-on and full-systems with a digital capability.

SOURCE: R. B. Emmitt and J. W. Lasersohn, "Company Report on Diasonics," F. Eberstadt & Co., Inc., New York, May 26, 1983.

NMR sales, in contrast, are expected to increase from $100 million per year in 1983 to $2.5 billion per year in 1988 (see tables 13 and 14 and fig. 11), an annual rate of growth in market size of 90 percent. According to this estimate, the percentage of industry sales attributable to sales of NMR imaging systems will increase from 2.5 percent in 1983 to 30 percent by 1988. The estimated rate of growth in worldwide NMR sales displayed in table 14 can be compared to a worldwide growth of X-ray CT unit sales of approximately 600 units per year over the first 5 years of X-ray CT availability (59). Most manufacturers with whom we spoke believed that the 50-50 percent split between U.S. and non-U.S. sales currently existing for X-ray CT systems will be observed for NMR sales as well.

It is useful to consider the assumptions on which the estimates are based. First, the estimates assume that, given the expected change to prospective systems of hospital payment, the hospital industry will be unable to bear a major increment in capital expenditures over the next several years. It is assumed, however, that although the rate of increase of *hospital* expenditures on imaging equipment may slow over the next several years, the slowing will be offset by increases in purchases by *private* radiology groups and that the recent growth in sales of diagnostic imaging equipment of 15 percent annually will remain constant over the next 5 years.

The second major assumption is that, at least in the near future, sales of NMR imaging systems will compete primarily with sales of X-ray CT systems. This situation is thought to be the case because both systems provide cross-sectional tomographic images with what is expected to be similar spatial resolution in the near future. The estimates therefore assume that many hospitals will be making decisions about purchasing *either* NMR imagers or X-ray CT scanners.[16]

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[16] This will also be the case for hospitals that have one or more X-ray CT scanners and are contemplating buying additional ones. In 1980, more than 100 U.S. hospitals had more than one X-ray CT

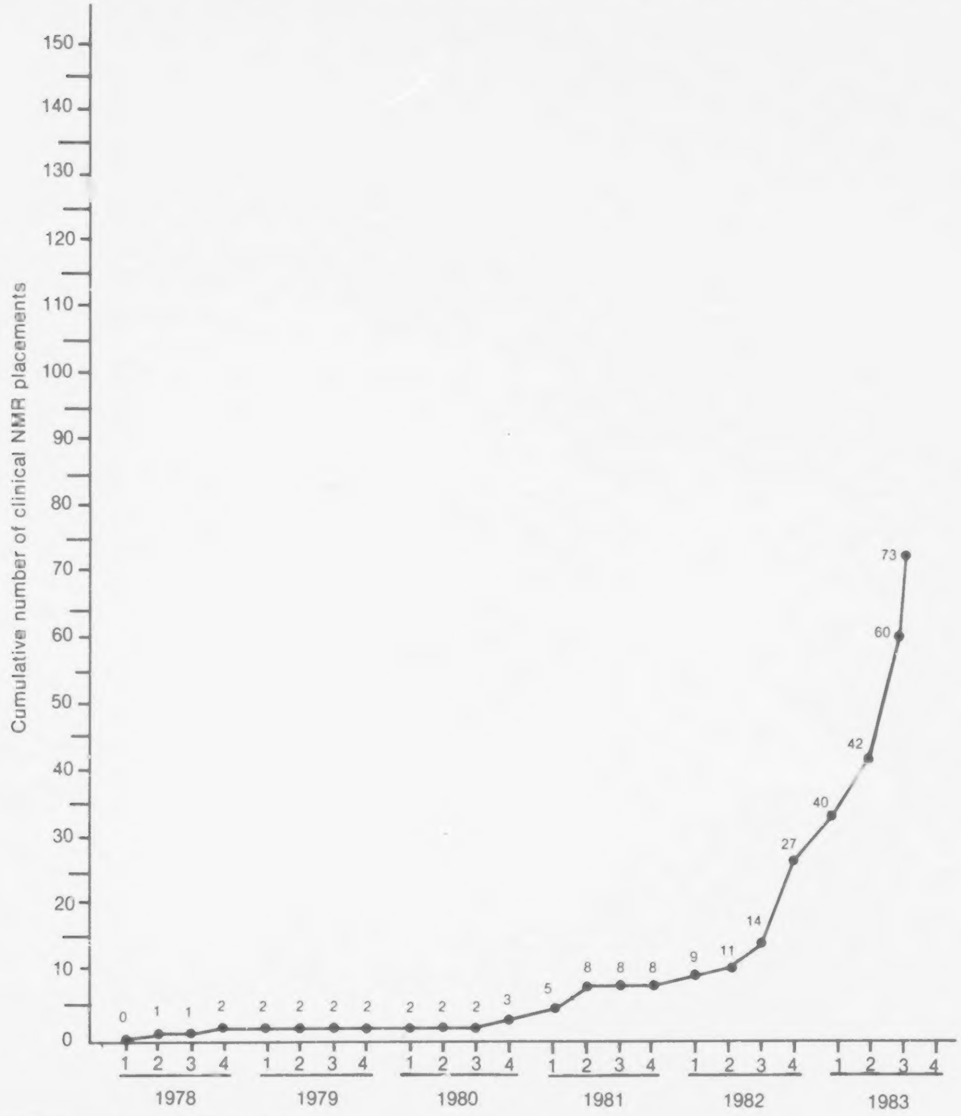
Table 14.—Estimated Worldwide NMR Market

Year[a]	Annual unit deliveries	Cumulative unit deliveries	Average sales price	Annual sales ($ million)
1982	15	15	$1,300,000	$ 20
1983E	75	90	1,300,000	100
1984E	200	290	1,500,000	300
1985E	400	690	1,600,000	650
1986E	650	1,340	1,700,000	1,100
1987E	905	2,290	1,850,000	1,750
1988E	1,250	3,540	2,000,000	2,500

[a] E = Estimated.

SOURCE: R. B. Emmitt and J. W. Lasersohn, "Company Report on Diasonics," F. Eberstadt & Co., Inc., New York, May 26, 1983.

Figure 11.—Cumulative Number of Worldwide Clinical NMR Placements Over Time



SOURCE: Interviews with NMR manufacturers.

The third major assumption is that, if NMR imaging did not exist, the growth in X-ray CT-guided procedures would increase the sales of X-ray CT systems by 10 to 15 percent per year. Given current, annual sales of 1,000 X-ray CT units worldwide, this assumption implies that, without NMR, there would be the potential for sales of 2,000 X-ray CT units per year in 1988.

The fourth assumption is that, in the NMR versus X-ray CT competition for this 2,000 unit-per-year market in 1988, NMR will capture 1,500 of the projected 2,000 unit sales. It should be

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scanner, and approximately 450 additional hospitals, all with more than 300 beds, had at least one X-ray CT scanner (59). Sixty percent of X-ray CT systems sold in the United States in 1982, in fact, were the second, third, or fourth systems acquired by a hospital (61).

noted, though, that while the model assumes that sales of NMR imagers will exceed sales of X-ray CT imagers in 1988, it does not assume that use of NMR will replace use of X-ray CT clinically in the near future.[17]

Finally, the estimates assume an annual inflation rate of 5 percent.

In addition to it being difficult to predict the magnitude and nature of future diagnostic imaging equipment sales, it seems equally hazardous at this time to project what the character of the NMR imager manufacturing industry will be 5 years hence. Although no predictions can be made regarding how many or which of the current NMR imaging manufacturers will be involved in the field in 1988, two general comments can be made. First, to the extent that "turf battles" between radiologists, nuclear medicine specialists, pathologists, neurologists, and cardiologists develop over control of NMR imaging and spectroscopy, the market shares of large X-ray manufacturing companies that are currently based on radiology franchises may decrease (60). Second, although the emergence of new imaging modalities was thought to be the primary challenge to major X-ray manufacturers in the 1970s, it is anticipated that the rapidly expanding role of data and image processing across all imaging modalities will become the major challenge to X-ray equipment manufacturers in the 1980s (60). To the extent that this does, in fact, become the case, future concentration or fragmentation in the diagnostic imaging market may, in large part, be determined by the responsiveness of large diagnostic imaging conglomerates to this anticipated trend (60).

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[17] It seems very likely that NMR will not replace X-ray CT in the near future. There may always be a role, for example, for X-ray CT in patients with metallic implants who will not be considered candidates for NMR, and for guiding biopsy or surgical procedures that employ metallic instruments. Furthermore, it is difficult to predict the extent to which X-ray CT scanning techniques will improve in the future. In the 10 years since X-ray CT scanners were introduced, their scanning speed has increased 300 times, their spatial resolution has increased 8 times, their density resolution has increased 3 times, and their radiation dosage to the patient has decreased markedly (15). In addition, new X-ray CT scanners are being developed that are capable of completing a scan in about 30 milliseconds, permitting performance of real-time cardiac X-ray CT imaging (15).

5.

Hospital Costs and Strategies

5.
Hospital Costs and Strategies

INTRODUCTION

One of the major concerns regarding NMR imaging relates to the impact this new technology will have on health care costs. This concern derives in part from the high costs anticipated for the purchase and installation of an NMR imaging system and uncertainties regarding the extent to which NMR imagers will be used in addition to, rather than instead of, other diagnostic modalities already in hospitals. The purpose of this chapter is to present a framework for addressing the cost issue. The chapter is organized into three sections. The first section presents data regarding the likely capital and operating costs of different types of NMR systems. The second section addresses other factors that will influence the effect of NMR imaging on patient care costs, and the final section describes the NMR acquisition strategies and decisions of different segments of the hospital industry.

CAPITAL AND OPERATING COSTS

Initial capital expenses and routine operating expenses for an NMR imaging system are primarily determined by the type of magnet used to produce the static magnetic field. Although insufficient experience has been accumulated to permit accurate predictions of the likely expenses of acquiring and operating an NMR imaging system, tables 15 to 17 attempt to provide the best available estimates of such expenses for four different types of NMR systems. It should be emphasized that the values provided in the following tables are *estimates*, and nothing more. They should therefore be interpreted in that spirit. Our purpose in presenting these estimates is to provide some indication of the factors that will contribute to the cost of operating NMR imaging systems and what total costs are likely to be, given reasonable assumptions.

In determining annualized capital costs, we have made the assumption that the useful life of the NMR imaging system itself is 5 years, while that of the site renovation is 10 years. A 10-percent interest rate has been employed. *Physician costs (i.e., professional fees) have not been included.*

Supply costs, estimated to be $15 per procedure, vary with the number of procedures performed per day. In the near future, while NMR remains investigational, it is probably reasonable to assume that no more than 10 procedures will be performed per day. By 1985 or 1986, it is reasonable to assume that 20 procedures per day will be performed on a single machine. If paramagnetic contrast agents come into use, supply costs will increase.

Maintenance costs are estimated to be either 5 or 7 percent of the purchase price. The former estimate is more reflective of the cost of maintenance performed by the hospital; the latter of the cost of maintenance provided by a manufacturer as part of a service contract. Given the absence of moving parts in NMR imaging systems, actual maintenance costs may be less than the estimates provided. Finally, overhead, which has been estimated to be 25 percent of operating costs, will vary from institution to institution.

As can be seen in table 15, purchase prices for permanent and superconducting NMR units tend to be higher than those for current generation X-ray CT scanners (estimated to be $600,000 to $1,200,000) (180,181). Based on the assumptions implicit in this analysis, including the performance of 10 procedures per day, the cost of an NMR imaging study in 1983 *exclusive of professional*

Table 15.—Range of Estimated Costs for NMR Imaging Systems by Type of Magnet, 1983

	Resistive (0.15 T)	Permanent (0.3 T)	Superconductive (0.5 T)	Superconductive (1.5 T)
Capital costs:				
Purchase price	$ 800,000[2][b] 1,200,000[1][c]	$1,500,000[1][4]	$1,500,000[2][b] 1,700,000[1][c]	$2,000,000[4]
Facility modification:				
Renovation		20,000 to 50,000[4]	150,000 to 250,000[4]	
New construction		50,000 to 75,000		
Unspecified modifications	150,000[3][b] 510,000[1][c]	75,000[6][b] 250,000[2][c]	650,000[1]	250,000[b] to 1,000,000[4][c]
Annual operating costs:				
Electricity (and cryogens[a])	$20,000[1]	$ 3,000[1][b]	$ 60,000[1][c]	$ 30,000[b] to 50,000[4][c]
	10,000[b] to 30,000[3][c]	8,200[6][c]	20,000[b] to 40,000[3]	
Personnel:				
Single shift	70,000[3]	70,000[3]	70,000[3]	70,000[3]
Double shift	140,000[3]	140,000[3]	140,000[3]	140,000[3]
Supplies ($15/procedure):				
10 procedures/day (2,500/year)	37,500[3]	37,500[3]	37,500[3]	37,500[3]
20 procedures/day (5,000/year)	75,000[3]	75,000[3]	75,000[3]	75,000[3]
Maintenance:				
5% of purchase price	40,000[2][b] 60,000[1]	75,000[1][4][b]	75,000[2][b] 85,000[1]	100,000[4][b]
7% of purchase price	56,000[2] 84,000[1][c]	105,000[1][4][c]	105,000[2] 119,000[1][c]	140,000[4][c]
Annual overhead:				
25% of operating costs	$39,375[d] to 82,250[e]	$46,375[d] to 82,050[e]	$ 50,625[d] to 98,500[e]	$ 59,375[d] to 103,750[e]

[a] Cryogens apply only to superconductive systems.
[b] Low estimate.
[c] High estimate.
[d] The lower estimates of operating costs are derived from the low estimates of electricity (and cryogens[a]) costs and of maintenance costs, as indicated. For personnel costs, a single shift and 10 procedures per day are assumed.
[e] The higher estimates of operating costs are derived from the high estimates of electricity (and cryogens[a]) costs and of maintenance costs, as indicated. For personnel costs, a double shift and 20 procedures per day are assumed.

SOURCES: [1] American Hospital Association, *Nuclear Magnetic Resonance Guideline Report*, AHA Hospital Technology Series, vol. 2, No. 8. (Chicago: AHA, 1983).
[2] W. H. Stephens, A. E. James, A. C. Winfield, et al., "Financial Implications of NMR Imaging," in *Nuclear Magnetic Resonance (NMR) imaging*, C. L. Partain, A. E. James, F. D. Rollo, et al. (eds.) (Philadelphia: W. B. Saunders, 1983).
[3] W. H. Stephens, J. A. Patton, J. E. Lagan, et al., "Certain Economic Considerations in NMR Imaging," in *Nuclear Magnetic Resonance and Correlative Imaging Modalities*, C. L. Partain (ed.) (New York: The Society of Nuclear Medicine, Inc., 1983).
[4] Interviews with manufacturers.
[5] E. F. Kuntz, "New Magnet May Lower Cost of NMR," *Modern Health Care* 106, January 1983.
[6] Fonar Corp., "Cost-Effectiveness in NMR Scanning: Making NMR Available to the Public at an Affordable Cost," October 1983.

Table 16.—Estimated Annual Costs for NMR Imaging Systems by Type of Magnet, 1983

				Resistive (0.15 T)	Permanent (0.3 T)	Superconductive (0.5 T)	Superconductive (1.5 T)
Annual capital costs:[a]							
Purchase[b]				$203,972 (800,000)	$ 382,447 (1,500,000)	$ 382,447 (1,500,000)	$ 509,929 (2,000,000)
Facility modification[c]				23,787 (150,000)	11,894 (75,000)	103,078 (650,000)	111,007 (700,000)
Total annual capital costs				$227,759	$ 394,341	$ 485,525	$ 620,936
Annual operating costs:[d]							
	Shift	maintenance	# procedures per day				
	Single	5%	10	$177,500	$ 190,700	$ 232,500	$ 267,500
	Single	5%	20	215,000	228,200	270,000	305,000
	Single	7%	10	193,500	220,700	262,500	307,500
	Single	7%	20	231,000	258,200	300,000	345,000
	Double	5%	10	247,600	260,700	302,500	337,500
	Double	5%	20	285,000	298,200	340,000	375,000
	Double	7%	10	263,500	290,700	332,500	377,500
	Double	7%	20	301,000	328,200	370,000	415,000
Range of operating costs				177,500 to 301,000	190,700 to 328,200	232,500 to 370,000	267,500 to 415,000
Annual overhead:							
25% of operating costs				44,375 to 75,250	47,675 to 82,050	58,125 to 92,500	66,875 to 103,750
Total annual costs				449,634 to 604,009	632,716 to 804,591	776,150 to 948,025	955,311 to 1,139,686

[a] Total costs on which annualized costs are based are in parentheses.
[b] Assuming 5-year useful life, 10 percent interest, and 60 equal monthly payments.
[c] Assuming 10-year useful life, 10 percent interest, and 120 equal monthly payments.
[d] The electricity and cryogens costs assumed (cryogens apply only to superconductive systems) were as follows (see table 15):

Resistive (0.15 T)	$30,000
Permanent (0.3 T)	$ 8,200
Superconductive (0.5 T)	$50,000
Superconductive (1.5 T)	$60,000

SOURCE: Table 15.

Table 17.—1983 Estimated Costs per NMR Imaging Study by Type of Magnet

	Resistive (0.15 T)	Permanent (0.3 T)	Superconductive (0.5 T)	Superconductive (1.5 T)
Single shift, 5% maintenance, 10 procedures per day:				
Annual cost	$449,634	$632,716	$776,150	$ 955,311
Cost per procedure	$ 180	$ 253	$ 310	$ 382
Double shift, 7% maintenance, 20 procedures per day:				
Annual cost	$604,009	$804,591	$948,025	$1,139,686
Cost per procedure	$ 121	$ 161	$ 190	$ 228

SOURCE: Table 16.

fees will likely range between $180 and $382, depending on the type of magnet system employed (see tables 16 and 17). However, Joseph P. Whalen, Chief of Radiology at The New York Hospital-Cornell Medical Center, New York City, recently estimated the cost of an NMR study as $700 (111), and recent industry estimates range from $382-$632 (66) to $500-$700 (159). This range of estimates derives from differences in underlying assumptions and suggests that it is too early to make cost-per-study estimates with much precision. In particular, lower estimates appear to reflect personnel and maintenance costs more typical of routine operations of a settled and defined technology, not of one still in an uncertain and developmental phase.

PATIENT-CARE COSTS

To consider only capital and operating expenses in a discussion of the fiscal impact of NMR imaging on hospital costs (or health care costs in general) ignores the effect of NMR imaging on patterns of patient management. Although physicians, hospital administrators, and health care researchers have alluded in the past to the importance of technology's effect on patterns of patient management, techniques for estimating the magnitude of a technology's effect on health costs are fairly primitive. With the advent of prospective, per-case systems of hospital payment, however, it has become increasingly important, particularly with regard to decisions to acquire new technology, for hospital managers to be able to explicitly assess the expected marginal cost of new services in relation to projected marginal benefits (102).

Regardless of the *potential* attractiveness of NMR imaging (or spectroscopy) as a diagnostic or research tool and the *potential* of NMR to be a cost-saving addition to physicians' diagnostic armamentarium, the *actual* impact of NMR on health care costs will depend not only on its diagnostic efficacy, but also on how it is employed by physicians in actual practice situations. Several factors should be considered in this regard. The first is the extent to which NMR imaging is performed instead of, as opposed to in addition to, other diagnostic modalities in the management of specific patient complaints or disease entities. It is possible, for example, that NMR will be used to assess the existence of lumbar disc protrusion in the evaluation of patients with low back pain, since it can provide excellent images of the vertebral column. To the extent that NMR imaging substitutes for the more invasive and risky technique of myelography (in which a radiopaque substance is injected into the spinal arachnoid space), NMR may decrease the cost of managing and increase the quality of care of such patients. To the extent that NMR is used in addition to myelography, however, NMR might improve patient care, but at additional expense.

A second determinant of NMR's impact on health care costs is the extent to which it will be used in situations in which no diagnostic modality is currently used.[1] Since NMR use does not involve radiation risk, such "newly induced" test usage may occur frequently. Consider, for example, the patient with low back pain alluded to previously. Patients suspected of having low back strain might in the future undergo NMR scans to confirm the clinical assessment of strain, rather than being treated with bed rest, heat, and analgesics without the use of any diagnostic imaging modality. Such use of NMR is likely to increase health care costs.

Two other potential newly induced test uses can be foreseen with the introduction of NMR. The first is "sequential NMR scanning" (see ch. 2) to monitor the natural history of disease in patients with atherosclerosis, multiple sclerosis, cysts, etc., in whom symptoms have either increased, decreased, or even not changed. The second is "sequential NMR scanning" to monitor therapeutic progress in patients being treated for cancer, infections, etc. The extent to which NMR will, in fact, be used in such a fashion should be determined by the sensitivity and specificity of the technique in each clinical application. The impact such usage will have on health care costs will depend on the as yet undemonstrated extent to which such usage decreases or increases total patient management costs in addition to improving diagnostic information or the quality of patient care.

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[1] This could be considered a special case of "add-on," with the patient history and physical examination being construed as diagnostic tests.

Recent analyses have suggested that over the past decade there have been striking increases in the amount of real inputs employed both per patient-day and per admission in U.S. hospitals (48). It is much too early to determine the aggregate effect of NMR imaging on patient care costs. Much will depend on such factors as how much surgery is avoided, whether hospital lengths of stay are shortened, and whether diagnostic workups that were previously performed in the hospital are shifted to the outpatient setting.

With the advent of prospective, per-case systems of hospital payment and increasing competition in health care, it is likely that those vested with the responsibility for making decisions regarding the acquisition of new technology such as NMR for hospitals will increasingly feel the force of two conflicting incentives. On the one hand, there will be the already mentioned fiscal pressure to be increasingly discerning of the patient care benefits compared to costs associated with acquisition of new technology. On the other hand, there will be pressure to offer the "best" and most recently available services in order to protect (or increase) an individual hospital's share of patients in the increasingly competitive market for patients. Whether and how hospital directors will obtain the type of information necessary to make such decisions may determine not only which hospitals survive in the current economic climate, but also the rate at which they acquire promising new technology such as NMR imagers.

HOSPITAL STRATEGIES

Introduction

Different segments of the hospital industry have employed different strategies for determining whether, when, and what type of NMR imaging equipment to buy. Each strategy and subsequent acquisition decision reflects the priorities of the hospital-industry segment or of particular hospitals within a segment and provides insights not only into technology assessment as practiced by hospitals, but also into hospitals' perceptions of the state of development of NMR imaging technology. An attempt has been made in this section to describe the acquisition strategies and decisions of three different segments of the hospital industry: university teaching hospitals and major medical centers; the Veterans Administration; and investor-owned hospital chains.

University Teaching Hospitals and Major Medical Centers

The Acquisition Decision

Most of the early NMR units acquired by hospitals have been installed in university teaching hospitals or major medical centers. This is not surprising given the interest such hospitals have in performing research and being at the "cutting edge" of medical developments, the manufacturers' need to have research performed in order to obtain FDA premarket approval, and the tendency of such hospitals to have large numbers of beds and a complicated mix of patients.

In addition to these forces driving university hospitals to acquire NMR imaging technology early on, several benefits that have accrued to those university hospitals that were among the earliest to acquire NMR imaging systems may help explain their acquisition decisions.

First, university centers have been able to use their special strengths to obtain NMR imaging systems from manufacturers at decreased or even no cost. Among the assets that university hospitals offer to manufacturers are: 1) their ability to provide a "laboratory setting" in which clinical data, needed by manufacturers for preparation of an FDA premarket approval application (PMAA), can be collected; 2) their special research talents in basic science, engineering, and clinical trial design, from which manufacturers have derived benefits in the form of improved system design, help with PMAAs, and publicity from publications in professional journals or presentations at professional meetings; and 3) the prestige associated with their institutions, which manufacturers' marketing divisions can convert into an effective form of advertising.

Second, because many of the university hospitals that were first to obtain NMR systems did so at little or no charge, they have ironically protected themselves from much of the cost associated with technological obsolescence.[2]

Third, the "price" and operating costs of these experimental systems are often partly subsidized by research grants provided to the hospital by the manufacturers.

Fourth, because many university hospitals have shared their NMR imaging systems with nonhospital university researchers, some of the acquisition expenses were often shared with the university. Finally, those hospitals and universities that obtained NMR imaging systems early are now in a position to capitalize on any research funds that will be awarded in early 1984 by the National Cancer Institute as part of its "Comparative NMR Imaging Studies" program (see ch. 6).

These observations suggest that many of the university hospitals that have obtained NMR imaging systems to date may have done so partly because they did not have to be so concerned with acquisition and early operating costs as other hospitals have to be.

Interestingly, in the case of NMR, a second opportunity to capitalize on university teaching hospital assets is now emerging for those hospitals that did not benefit the first time around. This second opportunity derives from the fact that increasing numbers of manufacturers are beginning to offer high field strength (1.5 T) NMR systems on which spectroscopic applications (an area in which many universities are replete with talent) need to be explored. These second-round hospitals can be expected to be fewer in number than those in the first round and are likely to obtain their benefits in the form of "two-for-one" bargains in which a 1.5 T system and a lower field strength system are obtained for close to the price of the lower field strength systems. Second-round buyers will benefit from the experience in site-planning gained by first-round hospitals.

Choosing a Manufacturer (or University)

Manufacturers have tended initially to install equipment in prestigious university centers. There is little information available on whether these first-round hospitals sought out the manufacturers or whether the manufacturers courted the hospitals. In some instances (such as Siemens and Washington University in St. Louis), installations have been a natural consequence of longstanding business relationships and research collaborations.

Several factors can be expected to influence university teaching hospitals' choices of manufacturers in future rounds of buying. Potentially most important are the hospitals' perceptions of a manufacturer's survivability in the NMR industry, the NMR system's features and capabilities, image quality, system reliability (up-time), manufacturers' interest in collaborative research, and the effect of a hospital's choice on its existing relationships with radiology equipment manufacturers. Potentially of lesser importance to university hospitals interested in performing research are price, protection against early obsolescence, and delivery time. To the extent that a research collaboration evolves, good service and technology upgrades (software and hardware) can be expected.

The Veterans Administration[3]

The Veterans Administration operates 172 medical centers nationwide in 6 regions and 28 districts on an annual medical service budget of $7 billion to $8 billion. Of these 172 medical centers 130 have onsite nuclear medicine services, and 80 to 90 have X-ray CT scanners.

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[2] Although NMR imaging systems will undoubtedly change over time, some experts believe that the changes in the hardware will be much less dramatic than those that have occurred with X-ray CT scanners. Aside from the *possibility* that low field strength resistive systems will become obsolete compared to higher field strength superconducting systems (which could be a concern for those "early bird" hospitals that acquired resistive systems), NMR systems may simply evolve through a continuing series of upgrades in software and minor changes in electronics (90). With X-ray CT scanners, in contrast, the entire set of electronics as well as the reconstruction algorithm, and other parts of the system are specific to the particular gantry being used. Thus, improvements have come in generations rather than through a process of simple upgrades (90). One other issue to be considered in this regard is that "early bird" hospitals might also have to redesign their facilities in the future to accommodate changes in magnet design or field strengths.

[3] The information in this section was drawn from a personal communication with S. Smith (171).

The VA central office must approve acquisition of technology costing more than $100,000 (a sort of "certification-of-need" (CON) analog). These high-cost items are apparently not considered part of the budgets allocated to individual hospitals, districts, or regions by the VA central office.

The NMR Decision

The VA's interest in acquiring an NMR imager originated in the VA central office rather than in one of its hospitals. In December 1981, after a presentation by an NMR manufacturer, VA elected to defer acquisition of an NMR system.

In early 1983, the VA decided to initiate what could become a program of staged acquisition with a single NMR demonstration and evaluation project. This decision derived from an interest in "helping the VA march into the future" (171). No estimates of the fiscal impact of NMR on the cost of patient care were made. The decision to restrict the initial purchase to a single unit emanated from a concern about the rapid rate at which NMR technology was changing and the desire to avoid installing a large number of systems that might soon become obsolete.

Choosing a Manufacturer

In early 1983, the VA solicited bids from manufacturers for a single system. No specifications were given regarding the type of magnet desired. Two bids, both for 0.15 T resistive magnet systems, were received.

Three factors guided the VA in its final choice of a system and manufacturer. First was a concern about manufacturer "corporate durability." (The VA regrets having bought six to eight X-ray CT scanners from Pfizer, which subsequently stopped manufacturing X-ray CT systems.) Second was evidence of a manufacturer's proven record of reliability in its already existing installations. Third was price.

Choosing a Site

The 0.15 T system obtained by the VA was to have been installed in the Cochran VA Hospital in St. Louis in October 1983. This decision was again made centrally with interest expressed by the Cochran VA. Three factors were considered in the choice of an installation site: the site had to have all other major diagnostic imaging modalities, a proven ability in high technology, and a good working relationship with the university with which it was affiliated. NMR expertise was desirable, but not necessary. CON controls were not a consideration because they do not apply to VA installations.

Site Operations

The NMR imaging system will be under the control of the hospital Chief of Staff, rather than being placed in either Radiology or Nuclear Medicine. This administrative decision was made to help foster the multidisciplinary team effort that the VA would like in its NMR program. Research protocols will be developed with input from the St. Louis staff, the VA central office, and outside consultants. The VA has not yet allocated monies specifically for NMR research. It should be recalled that the VA does not charge its patients. The VA will be getting a small research grant (approximately $75,000 per year for 2 years) from Technicare, the manufacturer of the VA's unit.

Future NMR Acquisitions

In June 1983, Dr. Donald Custis, the Chief Medical Director of the VA, formed a High Technology Assessment Group to determine what course the VA should follow with respect to acquisition of major new technology such as NMR imagers (e.g., what type, how many, over what time period).

Investor-Owned Hospitals

Humana[4]

Background.—Humana, based in Louisville, KY, owns or operates 92 hospitals. Humana has invested considerable effort in an assessment of NMR technology over the past 2 years. It has actively monitored NMR developments and discussed the technology frequently with manufacturers to help it decide what and when to buy. In addition, Humana has undertaken an interesting joint venture with Vanderbilt University. Through this arrangement, Humana obtains detailed information from Vanderbilt regarding NMR installation and operating costs, advice from Vanderbilt personnel regarding important questions to pose to manufacturers, and data from clinical studies. In return, Humana helps Vanderbilt obtain special consideration regarding price, software, and access to scientific and engineering expertise from the manufacturer(s) hoping to obtain a high-volume purchase agreement from Humana. (Humana conducted a similar joint venture with Vanderbilt before purchasing digital radiography equipment for Humana hospitals.) Humana is also providing a grant to Vanderbilt to assess the value of NMR in community hospitals.

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[4] The information in this section was drawn from a personal communication with F. D. Rollo (153).

The NMR Decision.—Although Humana has not made final decisions regarding what type(s) of and how many NMR systems to buy, it will probably buy in a phased approach, beginning with a purchase of three systems in the near future. Humana feels that such an approach will enable it to conduct an in-house evaluation of NMR, yet take advantage of future progress in the development of NMR imagers, particularly the possibility that permanent magnet systems will become more practical for smaller hospitals.

Humana's decision to acquire an NMR system(s) in the near future is based more on strategic considerations than on a belief that NMR's clinical role has been proven. These considerations are that Humana should not depend on either manufacturers or university hospitals to determine the optimal type of NMR system and NMR clinical applications in community hospitals.

Choosing a Manufacturer.—Humana identified seven criteria that it would employ in choosing a manufacturer: corporate durability, system quality, system reliability, how NMR information is related to the user, manufacturer agreements related to upgrading of a purchased system, quality of a service program, manufacturer's interest in collaborating with Humana's research interests, and price. Of these, price was considered to be the least important and corporate durability the most important.

Site Selection.—Humana considered three main criteria in determining which of its hospitals were appropriate for installation of NMR imaging systems. Appropriate hospitals were considered to be those with: 1) multispecialty practices with heavy emphasis on the neurosciences, oncology, and cardiovascular diseases; 2) high-volume outpatient services; and 3) adequate land for creation of an outpatient diagnostic center that would include, but not be limited to, NMR imaging equipment. In addition to these primary criteria, consideration was also given to the existence of NMR expertise among hospital staff and to whether NMR facilities would enhance the Preferred Provider Organization (PPO) and Health Maintenance Organization (HMO) programs Humana is developing. Finally, since Humana intends its NMR facilities to serve as community resources, it has sought to place them in areas with large patient populations.

Using these criteria in conjunction with in-depth financial analyses, Humana has identified three of its hospitals as appropriate for NMR installations: one each in St. Petersburg, FL (300 beds), Louisville, KY (484 beds), and Dallas, TX (600 beds). CON applications have been filed for two of these installations (the Louisville application was approved in September 1983), and a letter of intent has been filed for the third.

Site Operations.—Humana plans to undertake an educational program for the administrators and medical staff of the hospitals in which the NMR systems will be installed. These programs will deal with NMR in general and with physicians' use of NMR in diagnostic strategies. Access to an NMR system within a hospital will be governed by that hospital. Hospital administrators may undertake studies to evaluate the impact of NMR on the cost of managing various types of patients.

Future.—Humana could purchase as many as 12 NMR imaging systems over the next 3 to 5 years.

AMI Diagnostic Services, Inc.[5] [6]

Background.—AMI owns 90 hospitals and plans to build 50 to 100 freestanding diagnostic centers that will be affiliated with physician groups or hospitals. When considering the acquisition of new technology, AMI generally tries to assess whether the new technology will replace existing technology, whether it will do so at less cost, and whether it will shorten the length of inpatient stays. AMI requires an expectation of 20 percent return (pre-tax) on any of its investments.

The NMR Decision.—AMI started its strategic planning related to NMR technology in October 1982. It views NMR as safe and effective, especially in neurologic applications. It has questions, however, regarding the potential applicability of NMR to body imaging. AMI estimates that initial patient throughput is likely to be 10 to 15 patients per day per machine. Because of continued uncertainty regarding when reimbursement for NMR imaging will be approved, whether reimbursement for NMR will be sufficient to cover its costs, the safety regulations regarding siting requirements that State and Federal agencies will impose, and the impact a decision not to acquire NMR imaging technology will have on AMI's professional staff, AMI has not yet decided whether or when to acquire an NMR imaging system.

Choosing a Manufacturer.—The three most important criteria identified by AMI for choosing a manufacturer were perceived corporate longevity, service quality, and reliability (up-time) based on experience in existing installations. As was the case with other hospital chains, price was a less important consideration. Once the field is narrowed to manufacturers satisfying these concerns, AMI will leave the final decision to individual hospitals and physicians. AMI does establish national contracts for maintenance of its equipment, however.

Site Selection.—AMI identified four characteristics for determining which of its hospitals would be appropriate sites for installation of NMR imaging equipment: bed-size (greater than 250 beds), patient mix (heavy emphasis on neurologic and cardiac disease), large outpatient volume, and a dominant position in the community. Using these criteria, AMI currently considers 12 of its 90 hospitals to be appropriate for NMR installations and is applying for a CON in each of these cases.

Site Operations.—AMI does not intend to impose control over physician decisionmaking regarding use of NMR. It does intend, however, to implement a physician-education program pertaining to NMR and diagnostic-test-ordering strategy in general.

Future.—If AMI decides to purchase NMR equipment, it could purchase 50 to 100 units for its planned diagnostic centers and 12 units for hospitals, over a 24- to 36-month period.

National Medical Enterprises, Inc. (NME)[7]

NME owns, operates, or manages 339 acute, psychiatric, and long-term hospitals.

NMR.—NME began its strategic planning for NMR in October 1982. At the present time, NME does not plan to budget for NMR equipment until fiscal year 1986. It is maintaining close communication with manufacturers and with institutions that have already acquired NMR devices, however, to be aware of developments that might lead to a change in plans.

NME decided to defer acquisition of NMR technology because of its uncertainty regarding which magnet types and field strengths would prove to be most effective and whether separate systems would be required to perform proton imaging and spectroscopic analysis.

Site Selection.—NME has not decided which of its facilities would be appropriate sites for placement of NMR technology. It did believe that it would tend to put NMR imagers in its larger facilities, however.

Site Operations.—NME believes that NMR technology in the near future will be complementary to, rather than competitive with, X-ray CT.

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[5] An American Medical International, Inc., health care subsidiary.

[6] The information in this section was drawn from a personal communication with L. Atkins (10).

[7] The information in this sesction was drawn from a personal communication with D. Reynolds (152).

Lifemark[8]

NMR.—Lifemark owns or operates 30 hospital facilities. Since it began assessing NMR imaging technology in early 1983, Lifemark has attempted to keep abreast of NMR developments and to assess the instruments manufactured by various companies. It has made no decision regarding whether or when to acquire NMR imaging equipment, because it would like to be fairly certain that third-party payment is forthcoming before deciding to acquire NMR technology. It has as yet made no assessment of the likely impact of NMR on total patient-management costs.

Choosing a Manufacturer.—The major factors considered by Lifemark in any major equipment purchase are corporate durability, service commitment, and protection against technological obsolescence (as evidenced by manufacturers' ongoing R&D programs and willingness to supply software or hardware updates).

Site Selection.—Lifemark believes that the three hospitals it owns that have more than 300 beds and the one 300-bed hospital it has under construction will be the most likely early candidates for NMR imaging technology. Smaller hospitals that have a strong neurological or neurosurgical orientation would also be potential candidates. Lifemark's Columbia Regional Hospital in Missouri, a 300-bed general medical-surgical, multispecialty referral hospital, expressed an interest in obtaining an NMR unit over a year ago. Although the hospital received CON approval in March 1983, no definite purchase decision has been made.

Site Operations.—No definite decisions have been made regarding how NMR units would be utilized in hospitals. Any restrictions on NMR use would depend on the type of payment that is approved by third-parties.

Future.—Lifemark anticipates the possibility of purchasing four NMR imaging systems over the next 3 to 4 years.

Hospital Corp. of America[9]

Background.—Hospital Corp. of America (HCA) owns 150 hospitals and manages 150 others. It has an internal diagnostic-imaging technology advisory board that has traditionally taken a cautious approach to acquiring new technology. This approach has often resulted in HCA's getting new equipment up to 18 months after other hospitals. Recently, HCA decided that it would like to begin evaluating new technology such as NMR at an earlier point in the technology's evolution. This decision is based on the need to generate information regarding the likely role, operating costs, and patient throughput for new imaging technology in community hospital settings. (HCA has concluded that data emanating from university hospitals are not always applicable to their community hospitals.) In addition to recognizing the need for this type of information, HCA believes that it has sufficient numbers of 300- to 400-bed hospitals to be able to generate this information internally and that such information could help manufacturers obtain FDA and third-party payment approval.

The NMR Decision.—With this strategy in mind, HCA has decided to purchase five NMR systems—one 0.15 T resistive system, three 0.5 T superconductive systems, and one permanent-magnet system—from four manufacturers (Technicare, Picker, Philips, and Fonar), enabling HCA to evaluate several different magnets and manufacturers simultaneously. Each of the five hospitals earmarked to receive an NMR unit has analyzed the likely financial impact of introducing NMR on its patient care costs.

Choosing a Manufacturer.—HCA considered several factors in choosing the manufacturers: perceived corporate durability; maintenance capabilities; expected delivery time; and interest in HCA's research programs, as manifested by a willingness to supply onsite product specialists to help HCA evaluate instruments in community hospitals and to ensure that HCA obtains software updates. In general, HCA likes to obtain equipment from at least two, but not more than three, preferred manufacturers. HCA believes that such a strategy helps ensure against a manufacturer's "getting lax" in service and being unable to accommodate all of HCA's needs. Within this limited range of potential manufacturers, HCA permits each of its hospitals to make its own acquisition decision.

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[8] The information in this section was drawn from a personal communication with K. Harville (82).

[9] The information in this section was drawn from a personal communication with K. Bird (16).

Site Selection.—HCA considered four primary criteria in choosing the five sites for initial installations: bed size (250 to 400 beds); type of hospital (acute-care hospital with a large nearby clinical referral base and a sophisticated emergency room capable of handling trauma patients); type of patient-mix (with neurology, oncology, cardiology, and orthopedics emphasized); and degree of sophistication of the hospital's imaging department. On the basis of these criteria, HCA decided to install three units in 400-bed hospitals and two units in 250-bed hospitals.[10] Each of these hospitals have either applied for or are in the process of applying for CON.

Site Operation.—Each NMR facility will be operated as a separate cost center to improve the quality of financial information pertaining to the use of NMR. NMR units will be installed within imaging departments, which include both Radiology and Nuclear Medicine. Physician education programs will be prepared. The various NMR facilities may have different clinical emphases, depending on manufacturer needs.

Future.—The first stage of HCA's evaluation will involve five or six installations. Over the next 5 years, HCA could obtain as many as 25 to 50 NMR imaging systems.

Conclusions

Organizations that own or operate multiple hospitals seem to be employing two different strategies regarding acquisition of NMR imaging equipment. The first strategy is to obtain one or more NMR imaging systems as part of an in-house evaluation project to guide future decisions regarding acquisition of the technology. The alternative strategy is to defer any acquisition until additional information about NMR is available. What is clear is that no one considers it advisable to make large-scale purchases of NMR imaging equipment at this time. Although all hospitals are concerned about the impact of NMR on total patient management costs, only Humana and HCA appear to have conducted a formal, patient-management, cost-impact assessment. Finally, while many university teaching hospitals are able to use their prestige to obtain "favored status" from manufacturers, companies that operate chains of hospitals are able to elicit special consideration from manufacturers because of their buying power. The VA could capitalize on its potential to make high-volume purchases by following HCA's approach of designating a small number of preferred manufacturers.

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[10] The five hospitals are Chippenham Hospital in Richmond, VA; Medical Center Hospital in Largo, FL; West Florida Hospital in Pensacola, FL; Coliseum Park Hospital in Macon, GA; and Parkview Hospital in Nashville, TN.

6.

History of Funding for NMR Research

6.
History of Funding for NMR Research

INTRODUCTION

Government policies related to funding of medical device research and development by universities and manufacturers can have important impacts on the evolution of technology and the shape of particular device industries. The purpose of this chapter is to review the history of government funding for NMR research in the United States and in England and Scotland where much of the early work on NMR imaging was performed. Policy issues that emerge from this review are discussed in the final section of this chapter.[1]

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[1] Readers who are not interested in the details of government funding of NMR research may want to read only the final section of this chapter.

UNITED STATES

National Institutes of Health

Over the past decade, the National Institutes of Health (NIH) have supported research relating to NMR imaging, biomedical applications of NMR relaxation-time parameters, and biomedical applications of NMR spectroscopy. Although NIH has provided some funds for the development and use of software and ancillary hardware, NIH has not provided, and does not plan to provide, support to clinical or research institutions to be used either to develop or purchase NMR imaging machines for use in human imaging.

Intramural Research

Conventional Spectroscopy.—NIH has had an active intramural program of research involving conventional chemical and physical applications of NMR spectroscopy for many years. A description of these activities is beyond the scope of this report.

Instrumentation and Imaging Techniques.—Dr. David Hoult, a physicist and electronics engineer formerly involved with in vivo phosphorus spectroscopic research at Oxford University, has been at the Biomedical Engineering and Instrumentation Branch of NIH since 1977. Over the past 6 years, his research at NIH has focused on NMR imaging instrumentation and techniques. In addition to developing the rotating frame technique of NMR imaging (94) and systematically exploring the parameters affecting image quality, resolution, contrast and signal-to-noise ratio, Hoult has built a small-bore (30 cm diameter) 0.117 tesla (T) NMR imager. The imager as yet has been used only to image phantoms, but may be used for studies of animals or newborns in the future.

Physiology.—Dr. Robert Balaban, Senior Staff Fellow at the National Heart, Lung, and Blood Institute, has been studying physiological applications of phosphorus, sodium, and nitrogen NMR spectroscopy for the past 3½ years. In his research at NIH Balaban has employed in vivo ^{31}P NMR spectroscopy to measure the phosphorus content of cardiac muscle under varying physiological conditions, has measured the kinetics of metabolic reactions such as the transfer of phosphorus from adenosine triphosphate to creatine phosphate, and has studied sodium transport across plasma membranes and the concentration of various nitrogen-containing buffers in various tissues in the body.

Clinical Research.—Using funds contributed from many of its Institutes, NIH has purchased a 0.5 T whole-body NMR imaging system from Picker International. This system has been delivered to NIH and clinical studies were scheduled to begin in September 1983. This system, which was slated to be placed in the Department of Radiology, will be utilized by several Institutes to carry out research protocols approved by an

NIH NMR Users Committee. Initial studies will be done at a magnetic field strength of 0.15 T and will include investigations of demyelinating disease, the effects of chemotherapy and radiation therapy on NMR parameters, and whether NMR can be used to predict patients' responses to chemotherapy and radiation therapy.

Cellular Metabolism.—A fifth NMR research group has been formed at NIH by Charles Meyers, Chief of the Clinical Pharmacology Branch of the Division of Cancer Treatment at the National Cancer Institute (NCI). This group will be exploring the use of NMR in the study of the metabolism of both normal and cancer cells, as well as the effect of various drugs on cellular metabolism. The group will also be exploring possible applications of NMR to the study of the development of tumors (37).

Meyers' group will be drawing on the expertise of Dr. Jack Cohen, an NIH veteran of 15 years, whose research has focused on biochemical applications of NMR. Over the past 3 years, Cohen has used NMR spectroscopic techniques to study cellular metabolism (67), proteins, DNA conformation (34), and drug binding, including the binding of the chemotherapeutic agent Adriamycin to specific DNA sequences. Cohen has recently developed a method to perfuse living cells in an NMR spectrometer (68), which he has used to study ATP metabolism in mammalian cells (Chinese hamster lung fibroblasts).

Extramural Research: Past

NIH-Supported NMR Spectroscopy Research Facilities.—Although a complete description of NIH-supported, conventional NMR spectroscopic research is beyond the scope of this report, mention should be made of a number of NIH-supported NMR-spectroscopy research facilities around the United States that are devoted to the study of biological molecules. These include the Middle Atlantic NMR Research Facility at the University of Pennsylvania, the Western Regional NMR Biomedical Facility at the University of Utah, the Stanford Magnetic Resonance Laboratory, the Purdue Biochemical Magnetic Resonance Laboratory, the NMR Facility for Biomedical Studies in Pittsburgh, and the Francis Bitter National Magnet Laboratory at the Massachusetts Institute of Technology (190). The MIT National Magnet Laboratory, run by Dr. Leo J. Neuringer, is a national resource that makes available high field NMR spectrometers to biomedical investigators.[2]

NMR Imaging.—Although a few of the NMR-related extramural grants that have been funded by NIH over the past decade have been funded by the National Heart, Lung, and Blood Institute (NHLBI) (e.g., research by Lauterbur in 1975 related to the use of NMR imaging to study blood flow and about $200,000 per year provided to Lauterbur by NHLBI since 1978) and other Institutes, most of them have been funded by NCI. The first extramural NCI grant related to NMR imaging was awarded to Lauterbur at SUNY-Stony Brook in 1973 after publication of his landmark article (115). The award was made to help Lauterbur further develop his technique of NMR imaging and investigate its application to cancer research. His initial funding of approximately $100,000 per year for 3 years has been renewed at an approximately constant level, without interruption, since 1973. NIH also supported early work on T_1 measurements of surgically excised human tumors (45,46) and tumors in mice and rats (85,92), as well as on the imaging of tumors in live animals (44).

Extramural Research: Present

NIH is currently funding approximately $2 million of research relating to NMR imaging and/or in vivo spectroscopy in at least 10 different institutions (204). A complete description of the content of this research is beyond the scope of this report. The Department of Energy has awarded an additional $1.8 million for NMR-related research (204). It should also be noted that in 1983, NIH began providing support for innovative research performed by small businesses in a program similar to the one sponsored by the National

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[2] Of interest is the fact that IBM has recently supplied several million dollars to the Brigham & Women's Hospital in Boston, the University of California at Berkeley, and the MIT National Magnet Laboratory for a joint research program aimed at addressing basic biological and medical questions and developing a high-field, whole-body magnet with sufficient field homogeneity to permit performance of in vivo ^{31}P spectroscopy (1).

Science Foundation (197). No information was available regarding whether support has been provided for NMR research under this program.

Extramural Research: Future

The dramatic advances over the past decade in diagnostic imaging technologies, many of which can assist clinicians in diagnosing multiple types of pathologies, have created the need for comparative performance studies to clarify how our expanding diagnostic imaging arsenal can be used most effectively and efficiently. In October 1981, the NCI expanded its focus beyond supporting research directed principally at cancer detection and diagnosis by forming a Diagnostic Imaging Research Branch to advance the art of imaging all types of morphologic and functional pathologies.

In October 1982, this Diagnostic Imaging Research Branch announced a solicitation of proposals (191) for the performance of studies: 1) to explore and define the current and potential usefulness of present-day NMR imaging systems in clinical applications; 2) to establish optimal imaging conditions for NMR use in specific clinical problems; and 3) to carry out comparative performance and evaluation studies to determine the capabilities and limitations of NMR imaging systems in comparison with other modalities for clinical applications in human subjects in the detection, imaging, quantification, and diagnosis of morphological and functional pathology and in the noninvasive characterization of tissue (191).

The other techniques with which NMR is to be compared could include, but are not limited to, conventional X-ray imaging, computed tomography (CT), ultrasonic imaging, and radioisotope imaging, including single photon emission computed tomography (SPECT), and positron emission tomography (PET). Awards are to be for 3 years and are in the form of cost-reimbursement contracts. Announcements of awards, originally scheduled for June 1983, were made in mid-1984 (144).

There were three minimum requirements for qualification for an award: award recipients must own or have available a working NMR-imaging system of sufficient size and image quality for meaningful whole-body or head studies of human subjects; recipients must have access to equipment to carry out comparative imaging with one or more of the other techniques listed previously; recipients must be capable of imaging at least 150 patients in the first year and at least 200 patients in each of years 2 and 3 (191).

NIH is also planning to issue a Request for Applications for grants to study the physical, chemical, and biological bases for T_1 and T_2 relaxation times to gain further insight into the information implicit in these parameters. Although a 3-year program, with up to $1 million in grants in the first year, is being considered, no funds have actually been approved (144).

NIH is also considering the possibility of funding a small number of training fellowships in NMR (144).

National Science Foundation

The National Science Foundation (NSF), an independent agency of the Federal Government that supports basic research in 18 different scientific subject areas, supported a pioneering research project in NMR imaging through its Research Applications Directorate (Instrumentation Technology Program) during 1977-79[3] as well as a 3-year ($95,000) project by Lauterbur related to microscopic NMR imaging. NSF currently has no programs that support research in NMR imaging per se. However, NSF has provided, and continues to provide considerable support for investigations relating to digital signal processing, two- and three-dimensional analyses and image reconstruction, as well as other scientific principles on which NMR imaging is based (49).

NSF Regional Instrumentation Facilities

In 1978, NSF initiated a program designed to improve the quality and scope of research conducted in the United States by making sophisticated instruments broadly available to researchers in both academia and industry (196). This program of Regional Instrumentation Facilities was predicated on two beliefs. First, there was thought to be a growing need for researcher access to the powerful scientific instrumentation that had evolved out of recent advances in electronics, but which unfortunately was affordable by only a few research institutions. Second, it was thought that a program of instrumentation sharing might encourage interaction and cooperation between researchers from scientific disciplines that do not ordinarily collaborate with one another (150).

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[3] There was $309,500 awarded under grant #APR-7708185, "In-Vivo Nuclear Magnetic Resonance of Flow Patterns" to the University of California at Berkeley in 1977.

By November of 1979, NSF had awarded a total of $11,392,000 to eight universities in seven States for the establishment of such regional instrumentation facilities (196). Of the 14 grants awarded during the first 2 years of the program, 5 went to universities to establish facilities for the performance of high-resolution NMR spectroscopy, at a cost of over $5 million.[4] Researchers in these instrument facilities used the NMR spectrometers in a broad range of physical, chemical, biochemical, biophysical, and molecular biologic experiments. No NMR imaging instruments were installed in the facilities and no imaging research was performed. No information is available regarding the extent to which the spectroscopic research performed in these facilities was pertinent to the later development of NMR imaging techniques.

NSF also provides institutional support to the National Magnet Laboratory at the Massachusetts Institute of Technology.

Small Business Innovation Research Program

Although NSF directs most of its research support to basic scientific and engineering projects at academic institutions in the United States, since 1977 it has also operated a Small Business Innovation Research (SBIR) program. This program encourages science-based and high-technology small businesses with strong research capabilities in applied science, basic science, or engineering to submit proposals pertaining to research in scientific or engineering problems that could lead to significant public benefit (197). Three primary objectives of this program are to stimulate technological innovation in the private sector, to increase the commercial application of NSF-supported research results, and to increase the national economic and social benefits derivable from Federal research investments (197).

Awards under the most recent SBIR program solicitation were to have been announced in January 1984. Research proposals pertaining to: 1) the application of superconductivity to electronically oriented industries; 2) improved NMR probes; and 3) new procedures for NMR data display have been particularly encouraged. NSF expects to award about 100 Phase I (feasibility study) grants of up to $35,000 each. One-third to one-half of Phase I awardees will receive Phase II grants, which will cover 2 years of research and are expected to average $200,000 each.

NSF and ACR Research Workshop

In November 1982, NSF and the American College of Radiology (ACR) sponsored an engineering research workshop for engineers, physicists, computer experts, physicians, product developers, and business managers to identify critical gaps in imaging knowledge that require engineering support and to examine how engineering researchers, medical scientists, and clinicians could develop effective collaborative relationships out of which advances in radiological imaging might emerge (49).

In addition to identifying areas in which basic imaging research is needed, the conference attendees addressed the current research and development roles of various elements along the research-development-production-application continuum. They concluded that the medical imaging-system manufacturers perform little of the basic research on which advances in imaging technologies depend:

> . . . The instrument producer functions largely as a designer/integrator of high technologies into functional systems, taking the knowledge resulting from research done elsewhere and converting it into clinically useful imaging systems (49).

The need for additional sources of support for basic research was underscored.

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[4] NMR spectroscopy centers were established at Colorado State University, the University of South Carolina, the California Institute of Technology, the University of Illinois, and Yale University.

ENGLAND AND SCOTLAND

Between 1973 and 1983, at least three different noncommercial entities provided financial support for NMR research in England and Scotland. Between 1974 and 1979, the Medical Research Council, the British analog of our NIH, provided support to three different groups. Two of these groups were based at the University of Nottingham, one under the direction of Professor Peter Mansfield, the other under Professor Raymond Andrew. The third group was based at the University of Aberdeen in Scotland, under Professor John Mallard. Andrew's and Mallard's groups received support from the Medical Research Council between 1975 and 1978; Mansfield's group received support between 1976 and 1979.

In late 1977, the Wolfson Foundation, a private philanthropic organization in England, announced the availability of funds for medical research. Andrew's group at the University of Nottingham used funds received from the Wolfson Foundation between 1978 and 1980 to do NMR imaging research, including construction of a whole-body NMR imaging system.

Finally, the Department of Health and Social Security (DHSS) in England, through a program designed to support development of technology that might be of use in hospitals, also provided significant financial support for the development of NMR imaging technology. In 1976, DHSS provided funds to help establish an NMR research team at the London-based company EMI (29). A resistive magnet-based machine was built at EMI and head images were produced in 1978 (29). Following 2 additional years of developmental research, the EMI team constructed a superconducting, whole-body NMR imaging system, which was installed in Hammersmith Hospital in London in March 1981 (29). EMI also contributed funds to this development project.[5]

In 1981, NMR imaging began at the Hammersmith Hospital using the resistive NMR unit developed by EMI. DHSS apparently has also provided support to the clinical imaging program at Hammersmith, as well as support for NMR research to Professor Mansfield at the University of Nottingham (177).

RESEARCH AND DEVELOPMENT POLICY ISSUES

Certain differences between the history of the development of NMR imaging in the United States and Great Britain should be considered. In contrast to the NSF program's supporting basic research by small businesses on a broad spectrum of scientific and engineering problems (as opposed to product development research), the British Government attempted to develop technology that might specifically be of use in hospitals. This effort was focused through a program funded by DHSS that lent considerable financial support to the development of NMR imaging techniques. Comparatively little support for the specific development of NMR imaging technology was provided by the U.S. Government. However, once it became apparent that the development of NMR imaging systems was not only commercially viable, but also potentially extremely profitable, U.S. manufacturers rapidly and intensively began investing in NMR imaging development programs. In addition to applying their considerable electronics and engineering resources to this effort, U.S. manufacturers aggressively (and successfully) recruited scientists who had been actively involved in the early NMR development programs in British universities. Similarly, U.S. universities and hospitals have recruited British NMR scientists to help initiate and promote active NMR imaging research and development programs, contributing to what has become somewhat of a "brain drain" from Britain.

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[5] In approximately 1977, GEC of England independently began work on the development of an NMR imaging system. In April 1981, GEC acquired the Picker Corp. and formed Picker International by consolidating the Picker Corp., GEC Medical, and Cambridge Medical Instruments. In October 1981 Picker International Ltd. Division in England purchased EMI's NMR technology and program, including its program at Hammersmith Hospital.

Finally, in Britain there seem to have been several groups of physicists based in university settings who had background and interest in the development of NMR imaging techniques and who interacted and collaborated with medical researchers, clinicians, and each other. In the United States, in contrast, most of the early work on NMR imaging was done by Lauterbur and Damadian with apparently little, if any, interaction between the two, despite the fact that both were at SUNY campuses. In addition, there seem to have been fewer centers in the United States in which scientists with varied backgrounds collaborated on the type of interdisciplinary research that resulted in the NMR imaging advances in Britain. Perhaps the collaborations between physicists and physicians that are now developing as part of hospital- and university-based NMR imaging programs, as well as the recognized need for interdisciplinary research collaborations that emerged from the 1982 NSF and ACR research workshop, will change this situation in the future.

7.

Regulation by the Food and Drug Administration

7.

Regulation by the Food and Drug Administration

INTRODUCTION

NMR imaging devices are the first imaging devices for which the Food and Drug Administration (FDA) premarket approval has been required under the Medical Device Amendments of 1976. (Previous imaging devices, such as X-ray CT scanners, were introduced before the amendments were passed.) Because the FDA approval process can have such an important effect on the rate at which new technology is introduced into the health care system, it is important to examine how the FDA regulatory process operates and how a promising technology such as NMR imaging has fared in its encounter with it. This chapter is devoted to those two tasks.

The chapter is divided into three sections. The first section describes the statutory sources of FDA authority over NMR imaging devices. The second section describes the process through which new devices such as NMR imagers are brought to market. The section includes a flow diagram (fig. 12) that illustrates the process, and a summary of how NMR imagers have fared in each stage of the approval process. The final section assesses the premarket approval process as a whole and raises a number of policy issues that should be addressed in evaluating it.

SOURCES OF FDA AUTHORITY

Radiation Control for Health and Safety Act

FDA authority over NMR imaging devices derives from two Federal acts. The first is the Radiation Control for Health and Safety Act of 1968, established to protect the public from hazardous radiation emitted by electronic devices. Because no hazards deriving from electromagnetic fields have been identified with current NMR devices, FDA has not established any radiation emission performance standards for NMR devices under the authority of the Radiation Control Act. According to the Director of Electronic Products in FDA's Center for Devices and Radiological Health, ". . . it is not likely that the Radiation Control Act will have any significant impact on the development of NMR imaging as a medical diagnostic modality" (164). However, if defects were found in NMR devices that rendered them unsafe, FDA could use the authority of the act to recall them, even though no performance standards have been developed.

Food, Drug, and Cosmetic Act

The second source of FDA authority over NMR imaging devices is the Food, Drug, and Cosmetic Act as amended in 1976, which controls the introduction of medical devices into commerce. In contrast to the Radiation Control Act, the Food, Drug, and Cosmetic Act has had, and continues to have, a significant impact on the development of NMR imaging devices. The 1976 Medical Device Amendments require that all medical devices intended for human use be classified into three regulatory categories (classes) based on the extent of control necessary to provide reasonable assurance of the safety and effectiveness of each device.

Class I devices are those for which general controls relating to adulteration, misbranding, banning, notification, reporting, registration, restrictions on sale or distribution, and good manufacturing practices are considered sufficient to provide reasonable assurance of safety and effectiveness.

Class II devices are those for which general controls are considered insufficient to provide reasonable assurance of safety and effectiveness, and for which there is sufficient information to establish a performance standard to provide such assurance.

Class III is reserved for devices: 1) that are used in supporting or sustaining human life, are of substantial importance in preventing impairment of human health, or present a potential unreasonable risk of illness or injury; and 2) for which Class I and Class II controls are either insufficient to provide reasonable assurance of safety and effectiveness or for which insufficient information exists to establish a performance standard that would provide this assurance. Class III devices require premarket approval (PMA) from FDA.

Figure 12 provides a flow diagram that illustrates how a new medical device, such as an NMR imager, finds its way through the FDA process into commercial distribution. The following sections describe the illustrated process in more detail.

REGULATION OF NEW MEDICAL DEVICES UNDER THE FOOD, DRUG, AND COSMETIC ACT

Premarket Notification of Intent To Market a New Device

The Medical Device Amendments of 1976 include a provision titled Premarket Notification (sec. 510(k)), which was designed to ensure that manufacturers did not begin marketing new devices until such devices had either received premarket approval or had been reclassified into Class I or II. Under this provision, a manufacturer must notify the FDA 90 days before it intends to begin marketing a device that was not sold prior to May 28, 1976. At the time of this Premarket Notification, the manufacturer must also specify the class into which the device has been classified or state the fact that the device has not yet been classified.

Under the 1976 amendments, any new device is automatically classified into Class III unless it is deemed to be "substantially equivalent" to either a preenactment device (i.e., one introduced prior to May 28, 1976) or a postenactment device that has already been classified into either Class I or Class II.[1]

To our knowledge, no NMR imaging manufacturer has submitted a petition to FDA arguing that NMR imaging devices are substantially equivalent to either a preenactment device or a postenactment Class I or Class II device. NMR imaging devices thus are Class III devices that unless reclassified, cannot be marketed prior to approval of a premarket approval application (PMAA) or a Product Development Protocol before marketing (see below).

Getting a Class III Device to Market

As indicated in figure 12, a Class III device such as NMR imagers can be brought to market through one of several pathways: reclassification into Class I or II, initiated either by a petition or FDA; premarket approval; or Product Development Protocol.[2] Although NMR manufacturers considered reclassification, they have used the premarket approval approach.

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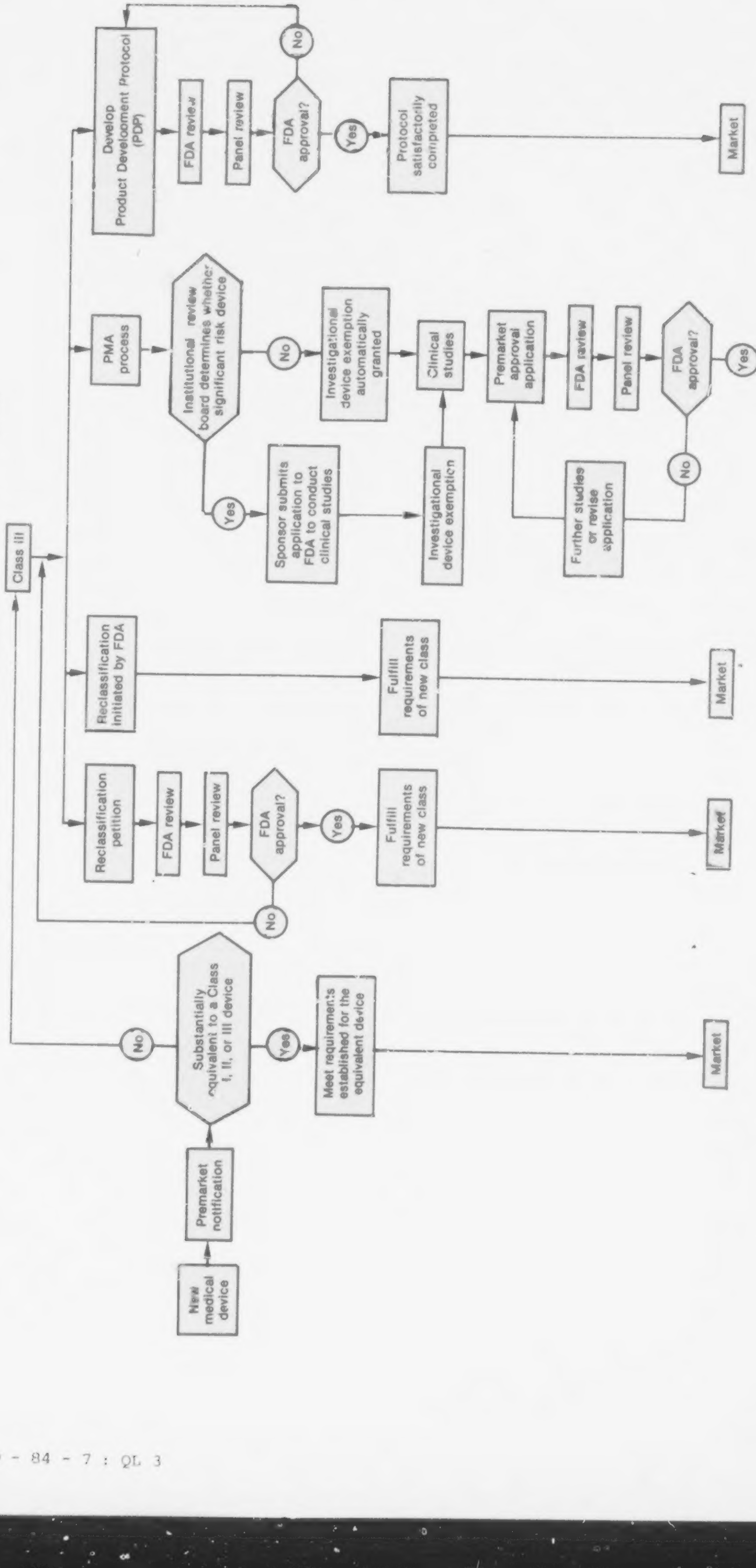
[1] If the new device is deemed to be "substantially equivalent" to a preenactment device, then the new device automatically assumes the classification of that preenactment device. Of significant importance is the fact that if a new device is deemed to be substantially equivalent to a preenactment Class III device, it may immediately be marketed without a premarket approval application.

[2] Under a Product Development Protocol, a manufacturer and FDA would agree on a plan of study to demonstrate reasonable assurance of the safety and effectiveness of a device. After receipt of a notice of completion of an approved protocol, FDA may declare the protocol completed or find that the results of the trials performed under the protocol differ substantially from the results required by the protocol, or that the results do not provide reasonable assurance of the safety and effectiveness of the device under the conditions of use in the proposed labeling. At least until December 1983, no manufacturer had elected the approach of a Product Development Protocol.

Figure 12.—How To Get a New Medical Device to Market


New medical device
Premarket notification
Substantially equivalent to a Class I, II, or III device
No
Yes
Meet requirements established for the equivalent device
Market
Class III
Reclassification petition
FDA review
Panel review
FDA approval?
No
Yes
Fulfill requirements of new class
Market
Reclassification initiated by FDA
Fulfill requirements of new class
Market
PMA process
Institutional review board determines whether significant risk device
Yes
No
Sponsor submits application to FDA to conduct clinical studies
Investigational device exemption
Investigational device exemption automatically granted
Clinical studies
Premarket approval application
FDA review
Panel review
FDA approval?
Yes
No
Further studies or revise application
Market
Develop Product Development Protocol (PDP)
FDA review
Panel review
FDA approval?
No
Yes
Protocol satisfactorily completed
Market

SOURCE: E. P. Steinberg, Johns Hopkins Medical Institutions, Baltimore, MD, 1983

Reclassification

According to the Medical Device Amendments of 1976, a manufacturer may petition FDA to reclassify a Class III device into either Class I or II. Reclassification petitions are referred to an expert advisory panel that within 90 days must recommend to FDA whether classification of the device in Class III is required to provide reasonable assurance of the device's safety and effectiveness. Within 90 days of receipt of the panel's recommendation, FDA must either approve or deny the petition.

On July 6, 1982, the National Electrical Manufacturers Association (NEMA), a trade association representing 13 companies involved in the development of NMR imaging systems and magnets, requested a meeting with FDA to discuss the possibility of initiating the reclassification process. At a meeting in December 1982, NEMA offered the view that NMR was an anatomical imaging modality whose safety and effectiveness were adequately assured by the General Controls of Class I. FDA expressed concern that NMR was a rapidly developing technology whose safety and effectiveness had yet to be demonstrated. According to the Director of the Division of Electronic Products in the Center for Devices and Radiological Health:

> The clinical possibilities for NMR imaging and the immaturity of its current applications were factors behind the FDA's opinion that Class III is appropriate for the modality. NMR's promise, while immense, is still unrealized. Clinical experience is still inadequate to establish effectiveness of specific NMR applications and to permit the development of adequate labeling, indications, techniques, and instructions. Each area of research will have to be studied scientifically and clinically to develop this information (164).

The official minutes of the December 8, 1982, meeting state:

> There were a number of concerns that the data presented left a clear impression that industry has not substantiated a general claim that NMR was an effective device that could be utilized across the spectrum as an imaging modality. It was further stated that it would be advisable for industry to start with a limited claim on the effectiveness of NMR with supporting scientific documentation . . . (It was further stated) that the Panel would review a reclassification petition if it were submitted in the appropriate legal manner (140).

No reclassification petition had been submitted as of December 1, 1983.

The NMR imager manufacturers that we surveyed were divided over whether it was redundant or wasteful to require that all manufacturers obtain PMA (see below). About half of the manufacturers felt that NMR imaging was sufficiently generic that once a PMAA was approved, FDA should set performance standards rather than continue the PMA requirement for each device. The other half of the manufacturers felt that NMR imaging is not "generic" because important differences exist between available NMR imaging systems, and that, consequently, each manufacturer should be required to obtain PMA (see below). These manufacturers argued in addition that the PMA process serves an important quality-assurance function and should be applied to all manufacturers. Although we think it is important to identify these two viewpoints, we lack sufficient information to comment on either the extent to which different manufacturers' NMR imaging systems do, in fact, differ, or the extent to which manufacturers' opinions reflect, in part, how close they are to obtaining PMA.

The Premarket Approval Process

In order to obtain premarket approval for a device, a manufacturer must provide reasonable assurance that the device is safe and effective under the conditions of use prescribed, recommended, or suggested in the proposed labeling. NMR imaging devices are the first imaging devices to have encountered this process. The following sections explain how the PMA process works and describe how FDA has applied the process to NMR imaging devices.

Significant Risk Devices

A manufacturer may place a device at an investigational site to collect data pertaining to safety and effectiveness. Such data can be collected according to a plan approved either by a local Institutional Review Board (IRB) (a local committee that reviews proposed scientific studies) or FDA. If the IRB approves the investigation as involving a nonsignificant risk device (one that does not pose serious risk to experimental subjects), the investigation is deemed to have an approved Investigational Device Exemption (IDE) and an application to FDA is not necessary. A sponsor need apply to FDA for approval to conduct clinical studies under an IDE only if an IRB has determined a device to be a "significant risk device," i.e., a device that presents a potential for serious risk to the health, safety, or welfare of experimental subjects. FDA does not maintain records of nonsignificant risk investigations and may not even be aware that such investigations are being conducted.

On February 25, 1982, FDA issued "Guidelines for Evaluating Electromagnetic Risks for Trials of Clinical NMR Systems" (188). The guidelines were issued by FDA to "provide assistance to sponsors of clinical investigations, researchers, and IRBs in determining when a clinical study involving an NMR device might represent a 'significant risk' under the Investigational Device Exemption . . . and to prevent submission of IDE applications [to FDA] when they are not necessary" (188). The guidelines related to details of NMR imaging that the FDA believed would be least familiar to the IRBs:

> On the basis of current information the bureau believes that a study which does not exceed these guidelines probably does not present an unacceptable risk in these three areas:
>
> 1. Static (Direct Current) Magnetic Fields—whole or partial body exposures of 2 tesla (T).
> 2. Time Varying Magnetic Fields—whole or partial body exposures of 3 T/second.
> 3. Radiofrequency Electromagnetic Fields—exposure to RF fields that result in a specific absorption rate that exceeds 0.4 W/kg as averaged over the whole body, or 2 W/kg as averaged over one gram of tissue. Studies that expose patients above these guidelines should be considered to pose "significant risk" (188).

It should be emphasized that in issuing these guidelines, FDA did not declare that NMR imaging was "safe." Rather, it stated that it was reasonable to proceed with investigations that adhered to these guidelines.

Ten months later in a December 28, 1982, memo to NMR manufacturers, the Director of FDA's Division of Compliance stated that ". . . over the past few months it has become clear that the intention of the guidelines has been widely misunderstood," and that ". . . it has been rather widely reported to us that the guidelines have been interpreted as limits for patient exposures in NMR imaging investigations . . . This is not our intent" (189).

In an effort to clarify this misunderstanding, FDA stated that:

> It continues to be our view that within the context of the present understanding of the biologic effects of electric and magnetic fields, the medical NMR imaging devices currently in investigational use span a range from those which require no detailed analysis to demonstrate that they do not meet the definition of significant risk to those which do require analysis to make such a determination. It is the purpose of the guidelines to provide some simple criteria for use in establishing that demarcation. No implication should be taken that a device which exceeds the guidelines should necessarily be considered a significant risk device (189).

Our survey of NMR imager manufacturers revealed that most manufacturers found FDA's promulgation of "Significant Risk Guidelines" to have been quite helpful, but expressed two strong concerns. First, although FDA has clearly described its guidelines as an aid to IRBs in making significant risk determinations and not as limits governing patient exposures, simply by virtue of their existence, the guidelines have inevitably tended to become product specifications with which manufacturers are loath not to comply. Second, the manufacturers felt that the FDA guidelines were "poorly conceived." For example, manufacturers suggested that the 3 T/second guideline pertaining to time-varying magnetic fields was uninterpretable in the absence of a specified pulse duration. (The National Radiologic Protection Board in Great Britain, for example, suggested a guideline of 20 T/second for pulses more than or equal to 10 millisecond in its 1980 guidelines.)

These two concerns relate more to a disagreement over the content of FDA's guidelines than to their issuance per se. It seems appropriate for FDA to have issued the guidelines. If their content is deficient (and we are not in a position to evaluate that issue), scientific experts could help to change them, and the process through which they were established could be reviewed to assure that it provides for adequate expert scientific input.

Regulations Pertaining to Investigational Devices

During the period in which a device is considered to be investigational (i.e., while it is being assessed under an IDE), manufacturers and investigators must comply with four regulatory prohibitions:

1. they may not engage in promotion or test marketing of the investigational device (21 CFR 812.7(a));
2. they may not commercialize an investigational device by charging the subjects or investigators more for it than the amount necessary to recover costs of manufacture, research, development, and handling (21 CFR 812.7(b));[3]
3. they may not prolong an investigation of a Class III device beyond the point where it has become apparent that premarket approval cannot be justified (21 CFR 812.7(c)); and
4. they may not represent an investigational device as being safe or effective for the purposes for which it is being investigated (21 CFR 812.7(d)).

In our survey of NMR imager manufacturers, two issues related to IDE regulations were identified. First, a number of manufacturers complained that other manufacturers were not adhering to the spirit of the IDE prohibitions on preapproval promotion and test-marketing of NMR imaging devices. Such behavior, these manufacturers asserted, created a situation in which all manufacturers were forced to either test-market and promote, or suffer while following the law. One manufacturer said that to avoid this situation in the future, FDA should limit the number of research sites in which manufacturers are permitted to install investigational devices. In a few instances, such as Neodymium YAG (Yttrium Aluminum Garnet) lasers, FDA has established guidelines for the numbers of patients and the length of followup required in studies of investigational devices (50). Other manufacturers, however, were pleased that FDA was not being more strict in its enforcement activities. They considered the existing situation to be an acceptable compromise between prohibitions and no prohibitions.

The second IDE issue raised by our survey pertains to the prohibition on making a profit from investigational devices. Although manufacturers voiced a preference for being able to make a profit during the IDE stage, most thought the existing prohibition was logical and reasonable in concept.[4] Furthermore, they suggested that, in the case of "high R&D cost" devices such as NMR imagers, it is difficult to recoup R&D expenses during the IDE stage because of the small number installed.

In a recent article, Anthony Young, a Washington, DC, attorney, concurred with the view that the IDE regulations should not present a problem to device manufacturers:

> Existing regulations allow a manufacturer to charge for investigational devices and thus to defray a portion of the expense involved in bring-

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[3] According to an undated policy statement issued by the Office of Radiological Health's Division of Compliance, ". . . investigators may charge a patient their normal physician's fee and the cost of scanning the patient, provided the scanning costs do not include a profit." The letter continues, however, that sec. 50.25(b)(3) of the informed consent regulation requires that "any additional cost to the subject that may result from participation in the research be included in the consent form where appropriate." FDA agrees that it is appropriate in this situation, since third-party reimbursement may not occur. (141).

[4] One manufacturer felt that the existing prohibition on profitmaking from preapproval devices disproportionately hurt small manufacturers. Small manufacturers, it was argued, generally are dependent on external sources of capital to fund research and development and do not fare well in their quest for funds when they are prohibited from demonstrating a profit. Others argued, in contrast, that what is required for success in external capital markets is profitmaking potential, rather than profits themselves. It would seem that without the prohibition on profitmaking during the IDE stage manufacturers would have less incentive to apply for PMA.

ing a new device to market. There is sufficient latitude in the regulations concerning publicity of availability of the device that the manufacturer can reach those practitioners who will eventually become customers. A manufacturer who is straightforward in his claims for his device and who does not attempt to circumvent regulations in an attempt to get a jump on competitors should have no problems with FDA (206).[5]

Clinical Studies

With an IDE in hand, manufacturers may conduct clinical studies to substantiate the safety and effectiveness of the devices they propose to market. Under Federal regulations, well-controlled investigations are the principal means used to establish the effectiveness of a device. However, according to the committee report accompanying the Medical Device Amendments, FDA is authorized to accept meaningful data developed under procedures less rigorous than well-controlled investigations when well-documented case histories assure protection of the public health or when well-controlled investigations would present undue risks for subjects or patients. This provision is not intended to authorize approval on the basis of anecdotal medical experience with the device or unsubstantiated opinion as proof of effectiveness (183).

During the preapproval period, FDA realized that manufacturers were concerned about how to establish the safety of NMR. FDA responded to this concern by exempting manufacturers from responsibility for submitting data on electromagnetic interactions in their PMA applications. FDA's actions and rationale were summarized by Mr. Schneider of the Center for Devices and Radiological Health:

> After considering the biological interactions of the fields used in NMR imaging, [FDA] concluded that the existing fundamental scientific uncertainties could not be resolved by experiments normally associated with device evaluation.
>
> In fact, it would probably be economically impractical for any individual sponsor to assume the financial burden of supporting the research necessary to make significant progress in eliminating these uncertainties. Further, it would seem unwise, with respect to societal benefits, to suspend the development and deployment of NMR imaging as a medical diagnostic modality pending substantial improvement in the understanding of the biological interactions of radiofrequency electromagnetic fields and static magnetic fields.
>
> From available information, no immediate acute effects are expected from exposure conditions prevailing in the devices under investigation. Further, it seems that whatever risks may be associated with these exposures will be small compared to the potential medical benefits of the modality. [Therefore], potential sponsors have been advised that they need not submit experimental data on electromagnetic biological interactions as part of the safety component of a premarket approval application. Each sponsor was asked to provide an assessment of the physical exposure conditions in its device. The FDA will conduct a continuing review of the risk potential of these exposures in light of developing scientific knowledge (164).

The Premarket Approval Application

When a manufacturer believes it has collected sufficient data to establish the safety and effectiveness of its device, it submits a premarket approval application (PMAA) to FDA. The PMAA must include:

1. a statement of the components of the device;
2. a statement of the principles of operation of the device;
3. a description of the methods used in the manufacture of the device;
4. a summary of investigations and information bearing on the safety and effectiveness of the device under the proposed conditions of use; and
5. specification of the claims, indications, and instructions with which the manufacturer proposes to label the device.

The type and breadth of the claims made in the proposed device label determine, in part, the scope of the research that must be performed prior to submission of a PMAA. As Schneider of FDA explains:

> Each claim that is made must be supported by adequate scientific and clinical research. This means that in broadening the range of claims for

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[5] Mr. Young's statement should in no way be construed as representative of FDA's viewpoint.

> a device, a sponsor increases the expense and effort necessary to secure premarket approval (164).

With regard to NMR, Schneider has stated that:

> . . . there is a natural temptation to be enthusiastic about all possible applications of the modality. Under the premarket approval process, this can be expensive when a device is as new as NMR imaging . . . Under these circumstances, a sponsor may wish to make claims that insure commercial viability of a system but that are not inordinately costly (164).

In November 1980, FDA published a "Guideline for the Arrangement and Content of a Premarket Approval Application" to aid sponsors in the preparation of such applications (187). According to those guidelines, a PMA application should include a description of the disease(s) or condition(s) that the device will diagnose and the patient population for whom the device is intended.

About half of the manufacturers surveyed stated that they would have liked more precise guidelines from FDA regarding the required content for a PMAA (e.g., how many patients need to be studied, whether studies need to be blinded, etc.); the others felt that sufficient guidance had been provided by FDA. Manufacturers who had received feedback from FDA on submitted PMAAs felt that FDA officials had been extremely helpful, fair, and reasonable in their review of PMAAs, particularly since NMR was the first Class III imaging device to go through the PMA process. A fairly common complaint from manufacturers, however, was that the PMAA format was unnecessarily tedious and complicated.

FDA Review

FDA is allotted 180 days to review and either approve or disapprove a PMAA *that satisfies all regulatory requirements*. During this review process, FDA customarily provides feedback to sponsors regarding possible deficiencies in their PMAAs. The underlined qualifier can thus take on significant importance, since FDA can stop the 180-day clock while a sponsor responds to or remedies the possible deficiencies that have been identified by FDA.

Panel Review

The Medical Device Amendments require that FDA refer each PMAA to an appropriate expert advisory panel which, after considering all data provided, makes a *nonbinding* recommendation to FDA regarding whether the PMAA at issue should be disapproved, approved, subject to certain modifications, or approved. On July 6 and 7, 1983, FDA conducted an open hearing of the Radiologic Devices Panel on three NMR device PMAAs submitted by Diasonics, Picker International, and Technicare. Picker's PMAA pertained to NMR imaging of the head and neck only, while Diasonics' and Technicare's pertained to NMR imaging of both the head and body. The panel considered all the applications "approvable" and voted unanimously to recommend approval of all three PMAAs, subject to various contingencies, such as making specified modifications in Site Planning Guides or labeling.

FDA Approval

The Medical Device Amendments state that a PMAA is to be denied if:

1. reasonable assurance is lacking that the device is both safe and effective under the conditions of use prescribed, recommended, or suggested in the proposed labeling;
2. the methods used in the manufacture of the device do not conform to Good Manufacturing Practices;
3. the proposed labeling is false or misleading in any particular; or
4. the device does not conform to a performance standard with which it is to comply.

In evaluating the safety and effectiveness of a device for PMA of a Class III device, FDA considers, among other relevant factors:

1. the persons for whom the device is represented or intended;
2. the conditions of use for the device, including conditions prescribed, recommended, or suggested in the labeling or advertising of the device, and other intended conditions of use;

3. the probable benefit to health from the use of the device weighed against any probable injury or illness from such use; and
4. the reliability of the device (21 CFR 860.7).

After having considered these factors, FDA regulations specify that:

1. *There is reasonable assurance that a device is safe when* it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks. The valid scientific evidence used to determine the safety of a device shall adequately demonstrate the absence of unreasonable risk of illness or injury associated with the use of the device for its intended uses and conditions of use (21 CFR 860.7).
2. *There is reasonable assurance that a device is effective when* it can be determined, based on valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results (21 CFR 860.7).

The safety and effectiveness of a device must thus be considered in conjunction with one another, since assurance of safety depends on an evaluation of effectiveness.

FDA issued formal premarket approval for NMR imaging devices manufactured by Diasonics and Technicare on March 30, 1984, and for head and neck imaging devices by Picker on May 10, 1984.

CONCLUSIONS: THE PMA PROCESS AS A WHOLE

The application of the PMA process to NMR imaging devices raises several issues. First is whether there should be a PMA process at all, and, if so, what benefits derive from it. Congress established the PMA process in 1976 in response to a perceived need for greater protection from unsafe, unproven, ineffective, and experimental medical devices. At least with regard to NMR imagers, the PMA process seems to have successfully addressed that perceived need. Although disagreements may exist over how much data should be required before PMA is granted, there seems to be a general consensus that the PMA process serves a useful function in assuring the safety and effectiveness of marketed devices. As one manufacturer stated, "The PMA process provides the discipline required to force manufacturers to develop information they ought to have."

The second general PMA issue relates to whether a separate PMA should be required for each clinical application of NMR or whether PMA should be granted for the technology as a whole. No clear consensus emerges on this issue. On the one hand, it seems possible that an imaging technology such as NMR may well prove to be effective in some but not all potential applications, suggesting that it would be reasonable for FDA to grant PMA on a clinical application, by clinical application basis, much as it does with drugs. On the other hand, it can be argued that as long as there is reasonable assurance that NMR imaging is safe and that NMR is effective, in the sense that it gives a fairly accurate representation of internal anatomy, pathology, or function, it should be up to physicians, rather than FDA, to decide which NMR applications are appropriate. Given some threshold level of demonstrated effectiveness, it would seem that the latter viewpoint is not only reasonable, but also may be the only feasible one for FDA to adopt, since FDA cannot control each application once NMR devices are installed.[6] How FDA resolves this issue may depend on the breadth of the claims made by manufacturers in their proposed labels.

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[6] Although it would not be feasible for FDA itself to enforce a restriction on the use of NMR to certain clinical applications, the absence of third-party coverage for uses not approved by FDA might effectively curtail such uses.

A third general issue relates to the manufacturers' costs for data collection and PMAA preparation and FDA's costs for reviewing the applications. The central question regarding the cost of the PMA process for the manufacturer relates to the amount of money that would not otherwise have been spent on the assessment of safety and effectiveness if the PMA process did not exist. Most manufacturers said the difference was "a negligible amount," with most of it associated with employment of study design consultants and clerical preparation of the PMAA itself. FDA estimated that by July 1983 it had expended about 800 person-hours of effort on reviewing the first three NMR PMAs submitted to it (163). These estimates do not suggest that FDA regulation of NMR devices has entailed high direct costs. To the extent that these assessments are accurate, there seems to be little at issue other than the possibility of streamlining the PMAA itself. To the extent that pertinent, well-designed clinical studies are performed that would not otherwise be funded by manufacturers in the absence of the PMA process, it would seem that the PMA process is serving a useful function.

Fourth, the question arises as to how much the PMA process has constrained development and early placement of NMR imagers. There is no indication that the PMA process has restrained development of the prototypes themselves. In addition, the great majority of NMR manufacturers that we surveyed in the summer of 1983, stated that if the PMA process had not existed, they would have placed few, if any more NMR imaging systems in hospitals than they had already because many manufacturers were still developing and refining prototype systems and had not yet begun full "assembly-line" production capable of meeting existing demand. FDA thus does not appear to be significantly delaying the introduction of experimental model NMR imaging devices into hospitals. In addition, it should be realized that manufacturers use the experience they gain during the IDE period to refine system designs before embarking on full-scale production.

The actual and potential impact of the PMA process may well change in the near future, however, as manufacturers emerge from the prototype development stage. Manufacturers have stated, for example, that many existing "orders" are contingent on the manufacturers' receiving PMA. If PMA is not granted in a timely fashion, these manufacturers may begin to experience delays in receiving revenues to cover their development costs.

Perhaps the greatest potential impact of the PMA process—stemming from its ability to confer a competitive advantage on manufacturers who have received PMA first—is yet to be seen. How much of a financial benefit, in both the short and long run, will accrue to NMR manufacturers who are first to obtain PMA may well help determine not only the future of the NMR manufacturing industry, but also the speed with which manufacturers pursue development of other new technologies that emerge in the future.

8.
Third-Party Payment Policies

8.
Third-Party Payment Policies

INTRODUCTION

As one of several important economic and social forces influencing the adoption and use of medical technologies in recent years, third-party payment policies have increasingly become a major focus of attention (12,100,157,200). Of great concern to many policymakers have been the incentives engendered by payment based on costs that have already been incurred. The general failure of such payment mechanisms to distinguish between cost-saving and cost-raising technologies has offered little incentive for hospitals to include efficiency among their capital investment objectives (100,200). Consequently, hospitals' decisions to acquire new technology have placed little emphasis on the comparative cost effectiveness of technology use in clinical practice.

The cost-based system of payment has also tended to reward institutions that increase their definable costs without necessarily improving quality of care, while simultaneously penalizing those that improve care with a concomitant reduction in operating expense (151,198). In view of these concerns, the Medicare program is beginning to pay hospitals according to a *prospective* payment system, with rates set in advance of the period during which they apply. This change has new implications for technology adoption and use.

This chapter addresses third-party payment policies and how they apply to NMR imaging devices. The first section addresses the types of policy decisions made by the major third-party payers and the processes by which they determine coverage and payment levels for new technologies. The second section discusses the history and current status of third-party payer decisions regarding NMR imaging. Readers familiar with the operations and policymaking processes of the major third-party payers may wish to read only the second section. Otherwise, the first section provides a foundation for understanding how policy decisions are made.

THIRD-PARTY PAYER DECISIONS

In setting policies for the payment of hospital and medical services involving the use of new medical technologies, third-party payers must wrestle with three questions:

1. Should they pay for such services?
2. If so, under what conditions or circumstances should they pay for them?
3. How much should they pay under specified conditions?

The first and second questions relate to policy decisions regarding *coverage* of new services and the specific conditions that may apply. The third question pertains to policy decisions involving the *reimbursement or payment level* permissible under specified conditions of service coverage. Together, these three questions represent a sequence through which all third-party payers must pass when formulating comprehensive policies toward medical technologies. Payers tend to differ, however, in their general procedures, methods of assessment, and decision criteria. Nevertheless, the end product in each case is a determination or policy statement intended to *guide* policymaking within the program or within member plans or companies.

Coverage Policies

When a new medical technology moves from the laboratory into the hospital, third-party payers must decide whether or not to pay for its use. For a device such as NMR that requires the Food and Drug Administration's (FDA) approval before marketing, the coverage question often arises before or concurrently with FDA review, as manufacturers or providers contact insurers about coverage policy before reimbursement claims are submitted. In the period prior to FDA premarket approval, the technology or device is considered "investigational," and third-party payers tend *not* to reimburse for clinical services performed with it. The critical decisionmaking period, therefore, is the time just after FDA premarket approval has been granted, when hospitals and other providers anxiously await third-party payers' decisions on both coverage and reimbursement level.

Medicare

The Medicare program may reimburse for only those devices, services, or procedures that are determined to be both "reasonable and necessary." In making this determination, the Health Care Financing Administration (HCFA), which administers Medicare, first considers whether FDA has found the device "safe and effective." In practice, HCFA generally does *not* approve coverage of a new device *unless* FDA has already approved it. HCFA considers it to be a necessary but not sufficient condition that a technology be "safe and effective" in order for it to be "reasonable and necessary." HCFA, however, will *not* necessarily approve coverage for all devices that FDA has approved, largely because the two agencies differ in their respective definitions of "effectiveness." FDA deems a technology "effective" if it does what the manufacturer claims it will do, whereas HCFA considers the effectiveness of the technology with respect to health outcome. Another important consideration in HCFA's decision is the stage or level of acceptance of the innovation by the medical community—i.e., the extent to which the technology has become an accepted part of clinical practice.

In the absence of a centrally established HCFA coverage policy for a particular medical technology, the fiscal contractors for the Medicare program may make their own coverage policy decisions. When questions regarding the safety and clinical effectiveness of a technology arise in the field, however, fiscal contractors may request that HCFA perform an assessment. Requests for technology assessments may also originate from outside groups, such as medical specialty societies and manufacturers (192).

Within HCFA, a coverage question is directed first to the Bureau of Eligibility, Reimbursement, and Coverage and its Office of Coverage Policy. HCFA may in turn seek the advice of the Public Health Service. This advisory role rests with the Office of Health Technology Assessment (OHTA) in the National Center for Health Services Research. The full assessment process generally requires 8 to 18 months to complete (106,107). The assessment process frequently coincides with the FDA premarket approval process and the two agencies often share available data and information. In making its coverage policy decision, HCFA is not bound by the Public Health Service recommendations.

HCFA does not give consideration to the cost effectiveness of a technology when formulating its coverage policy decision, but may do so later when making policy decisions regarding reimbursement or payment levels.[1] At its discretion, HCFA may place restrictions on the coverage of a technology rather than grant "blanket approval" for the technology as a whole. In the past, restrictions have sometimes been application-specific—i.e., reimbursement is provided only when the technology is used for specific clinical applications or diseases. In other instances, coverage restrictions have centered on specific service settings (e.g., only inpatient) or providers or practitioners (e.g., physicians only), or even manufacturers and their devices. For example, coverage of CT scanners was, at first, limited to only specific models produced by certain manufacturers (106,107).

Medicaid

The HCFA decisionmaking process, as described above for Medicare coverage policy, generally does not apply to the Medicaid program. Responsibility for making Medicaid coverage policy decisions rests with the individual States, which, at their own discretion, may choose to cover certain technologies or services not covered by Medicare. States may also devise their own coverage restrictions on technology use. In cases where a State program extends Medicaid coverage to technologies not covered by Medicare, the program may initiate its own internal technology assessment, utilizing its own staff and possibly a panel of outside experts. Alternatively, States may opt to refer technology-related inquiries directly to HCFA for potential assessment.

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[1] HCFA sometimes sets charges or allowable rates for a new technology based on previous charge experience with technologies that are clinical alternatives to the innovation in question (see discussion on reimbursement level decisions).

As with current Medicare policies, Medicaid will pay only for services and technologies judged "reasonable and necessary." Noncovered technologies receive no reimbursement under Medicaid.

Blue Cross and Blue Shield Plans

Although the national Blue Cross and Blue Shield (BC/BS) Association plays an important role in assessing new technologies on behalf of its member plans, each plan reserves the right to make its own coverage policy decisions regarding specific medical technologies or services. In making such determinations, individual plans generally require that a technology receive FDA premarket approval before considering reimbursement coverage for its use (47). FDA approval, on the other hand, does not automatically ensure BC/BS coverage; nor does HCFA approval of the technology as "reasonable and necessary" for Medicare beneficiaries. HCFA decisions, nevertheless, are scrutinized carefully by the plans.

When questions arise regarding coverage of a new technology (i.e., an individual BC/BS plan receives an inquiry, claim, or letter of intent from a participating hospital or physician), the plan will often contact the national Association and request assistance. An internal technology assessment process then begins to develop recommended coverage policy for plans to consider when making their respective policy decisions. The assessment process generally requires 4 months to 1 year to complete (47).

Unlike the policy *decisions* of HCFA regarding Medicare coverage, the policy statements issued by the national BC/BS Association are strictly *recommendations* or guidelines. The thrust of the BC/BS assessment process, therefore, is not to formulate policy with carefully delineated conditions of coverage, but rather to identify the important issues that plans must address and to present useful information that will aid local decisionmaking. An important aspect of this "information clearinghouse" function is the clarification of technical and clinical details relating to a specific technology's safety, effectiveness, clinical status, and appropriate use.

BC/BS employs a three-level scale of clinical status: 1) experimental—the technology has been used only in animal studies, 2) investigational—the technology has entered preliminary clinical use, and 3) accepted medical practice—the technology has gained general use in medical practice. Some BC/BS plans write broad exclusionary clauses in their contracts for "experimental/investigational" devices. Others prefer to deal with emerging medical technologies on a case-by-case basis, making it possible, but not likely, that some investigational devices may receive coverage, albeit for specific clinical applications or uses.

When formulating policy recommendations on coverage of new technologies, the internal review committees of the BC/BS Association take cost-effectiveness information into account. The information does not affect the recommendations directly, but rather is transmitted along with the policy statement to member plans. Plans are then free to weigh the information accordingly in their respective coverage policy decisions. Some plans engage in sophisticated assessment activities of their own. BC/BS of Massachusetts, for example, convenes an Interdisciplinary Medical Advisory Committee to assist it in making coverage decisions for new technologies (47). Other plans may instead conduct their own assessments or surveys of available information on new technologies. In addition, since many plans serve as Medicare fiscal contractors (i.e., administer Medicare claims for HCFA), they may either closely observe or participate in the HCFA assessment process.

Commercial Insurance Companies

Commercial insurance companies operate independently of one another and, therefore, make independent decisions regarding coverage of new or emerging medical technologies. When a question arises concerning payment for a technology whose safety and effectiveness may not be known, individual companies contact the Health Insurance Association of America (HIAA), a private organization that represents and serves the commercial insurance industry. HIAA membership includes 338 companies, which collectively provide approximately 85 percent of all non-Blue Cross, private health insurance coverage in the Nation (112).

The HIAA inquiry and assessment process is frequently conducted concurrently with the FDA premarket approval process, as well as with the technology assessment activities of other third-party payers, most notably HCFA and the BC/BS Association. Individual commercial insurance companies may, of course, supplement the information obtained from the HIAA process by undertaking their own assessment activities. Such independent efforts tend to be of a limited nature, often involving direct solicitation of expert opinion from the most relevant medical specialty groups.

In making coverage policy decisions, companies face the same choices encountered by other third-party payers—i.e., coverage without restrictions, coverage with restrictions, or no coverage at all. As with HCFA and BC/BS, commercial insurers view FDA premarket approval as a necessary but not sufficient condition for coverage of a new technology. Companies examine closely the policy decisions rendered by HCFA and by various BC/BS plans, but will not necessarily adopt them.

Reimbursement or Payment Level Policies

Once the question of coverage policy has been decided by a third-party payer, attention is focused next on the issue of appropriate or "reasonable" payment for provision of covered services. Although "reasonableness" is a concept with intrinsic meaning to all third-party payers, its operating definition in practice will vary among payers. Complicating the picture is the need for each payer[2] to set separate reimbursement or payment rates for the hospital or facility in which the technology will be employed and for the professional service fee of the physician. Both rates can vary by geographic area, by service setting (e.g., hospital versus physician's office), by physician specialty, by clinical application of the technology, and by the past experience and fee history of the individual practitioner.

Medicare

HCFA sets reimbursement rates for *covered* physician services based on what it considers to be "customary, prevailing, and reasonable" charges. In making these determinations, HCFA staff in the Office of Reimbursement Policy consider such factors as:

- *Where* the technology will be used—in the hospital, in the physician's office, or in some other setting?
- *How* the technology will be used—for what clinical applications or disease conditions?
- *By whom* the technology will be used—by physicians with what type or level of specialty training and/or experience?

"Customary and prevailing" charges imply that consideration is also given to: 1) the customary or usual fees charged by a given practitioner for similar or related services in the past, and 2) the prevailing fee (or market price) charged by physicians in the same geographic area and with similar training/experience for similar or related services. In the case of many new or emerging technologies, customary and prevailing charges are impossible to document since little clinical experience, if any, has been gained in the general medical community by the time an HCFA policy decision is made. In such instances, HCFA staff or individual Medicare contractors look to similar technologies and base their reimbursement or payment rates, at least in part, on past experience with established services. For example, assuming Medicare coverage is granted for NMR imaging, policy decisions on reimbursement level will likely be based, in part, on the previous history of charges for X-ray CT scanning.

Since October 1, 1983, HCFA has begun to pay hospitals prospectively for inpatient services on the basis of diagnosis related groups (DRGs).

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[2] Medicare does *not* set technology-specific payment rates for prospectively paid inpatient hospital services under Part A, but does set rates for physician services under Part B.

The payment for utilizing a given technology for a specific DRG is thus embedded within the established DRG cost per case. For the time being, Medicare is continuing to pay for the capital costs (e.g., acquisition expense, interest, rent, land costs, and other expenses) incurred for major equipment. The capital allowance will be based on the proportion of total hospital charges in some base year that is attributable to Medicare patients. Capital expenses will be treated in this "pass-through" manner for the next 3 years, or until capital costs are brought into the DRG payment rates. For *uncovered* services, HCFA would refuse to pay such pass-through capital costs.

Thus, a hospital that chooses to invest in new technology under the prospective payment system is at risk that the added patient-management costs induced by the new technology will result in financial losses. More specifically, if use of a new technology (either as a substitute for, or as an add-on to, some other modality) increases the average operating cost of a given DRG (or DRGs) to a level above the prospective payment rate established for that DRG (or those DRGs), the hospital will not recover its costs.[3] In addition, hospitals adopting and using an uncovered technology would not be reimbursed for associated capital costs, and would also stand to lose should their average operating costs in the DRGs that use the new technology exceed the approved DRG payment rates.[4] A decision to acquire and to use new technology under the Medicare prospective payment systems, therefore, may have serious implications for the financial well-being of a hospital.

Although HCFA will not need to establish a reimbursement rate for use of a new technology in the inpatient setting, it will need to establish payment rates for outpatient usage and for the professional fee associated with both inpatient and outpatient usage. The level(s) at which these payments are established could have a tremendous impact on the rate at which new technology is adopted in both inpatient and outpatient settings.

Medicaid

Medicaid reimbursement policy for new technologies generally is not tied to that of the Medicare program (107). Although Medicaid rates for *both* hospital care and physicians' services are set using many of the same criteria described above for Medicare, the relative weights of such factors will differ by State program, resulting in considerable variation in payment levels across the Nation.

Blue Cross and Blue Shield Plans

Once coverage for a new technology has been approved by a BC/BS plan, the criteria of "usual, customary, and reasonable" (UCR) fees are employed to set physician charges for services. Under this approach, considerable weight is given to past history and to the plan's experience with particular physicians (47). Individual plans differ, however, in their approach to payment for hospital services; some plans reimburse hospital charges; others pay only for costs. With emerging technologies, the lack of relevant technology-specific data or past experience often requires the plan to examine charges or costs for related technologies or services from which they can impute likely costs and set "reasonable" charges for the new service.

Commercial Insurance Companies

The general procedures and criteria used by independent commercial insurance companies in establishing allowable hospital rates and physician fee schedules are essentially similar to those described above for Blue Cross and Blue Shield Plans. Commercial insurers, however, tend to deal directly with the insured rather than with providers.[5] Within a given company, therefore, the reimbursement for a specific service is more likely to be standardized than it is within a BC/BS plan (112).

General Observations

These cost-based reimbursement policies for hospitals and fee-for-service payments to physicians have been criticized for their retrospective nature and for their inherent biases toward increased technology adoption (198,200). Because physician fees for new technologies cannot easily be tied to historic or prevailing charges, and because UCR fee schedules are not likely to be established until after such technologies have been introduced, payment for new procedures is often set high and rewards technology adoption. Retrospective cost- or charge-based reimbursement systems also give providers little incentive to distinguish between cost-saving and cost-raising technologies and may influence private physician groups to acquire new technologies without regard to their cost effectiveness. The widespread acquisition of X-ray CT scanners by private radiology groups, for example, may find its parallel in large-scale purchases of NMR imaging devices by such groups. In addition, the continuation of historical reimbursement policies for physician fees may provide physicians with incentives to overutilize technology even in the hospital setting.

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[3] Conversely, adoption of cost-saving technology that decreases the average operating cost of a given DRG (or DRGs) relative to the prospective payment rate would benefit the hospital, which is entitled to keep the savings that would be generated.

[4] Costs could potentially be recovered if payments exceeded costs for other DRGs or if costs were shifted to non-Medicare payers.

[5] This may be changing, as more commercial insurers begin to participate in the development of preferred provider arrangements with hospitals and physician groups.

HISTORY AND STATUS OF COVERAGE POLICY DECISIONS FOR NMR IMAGING DEVICES

During early 1984, increasing numbers of third parties began paying for NMR. By June 1984, at least 10 commercial insurers were paying for NMR as part of "generally accepted practice," and at least three Blue Cross plans had accepted NMR for payment.[6] Assessments of NMR imaging are being undertaken by HCFA/OHTA and by the BC/BS Association. The status of each payer's policy regarding NMR imaging is summarized below.

Medicare

HCFA became involved in the assessment of NMR imaging as early as January 1982, when the agency received literature pertaining to NMR from the General Electric Co., together with a request for comments, but *no* request for an assessment (17). In May 1982, HCFA received a formal query regarding Medicare coverage policy for NMR imaging from a Blue Cross plan in California, which had itself received an inquiry from a neurosurgeon (17). Acting on this inquiry, staff from the Office of Coverage Policy performed a literature review, contacted other Federal agencies (including FDA), surveyed NMR imaging manufacturers for information, and prepared a presentation to the HCFA Physician Panel in August 1982 (17). Later that month, the Physician Panel requested that OHTA perform a full assessment of NMR imaging. In September 1982, OHTA began to look at NMR but delayed a complete assessment pending FDA premarket approval. Recently, following FDA approval of the first manufacturers' applications, OHTA initiated efforts to assess NMR imaging. A decision by HCFA on Medicare coverage of NMR imaging is not expected during 1984.

Medicaid

Presently, it is not known whether State Medicaid agencies have conducted their own assessments of NMR imaging. It is possible that the current HCFA/OHTA assessment process may satisfy the information needs of the individual State Medicaid programs.

Blue Cross and Blue Shield Plans

In October 1982, national Association staff formally requested an assessment of NMR imaging. Later that month, the Medical Advisory Subcommittee reviewed the request and decided to initiate an assessment. At that time, the Subcommittee also designated NMR imaging as an "investigational device" for which *no* reimbursement should be provided. The staff then performed an assessment and reported its findings to the Subcommittee in March 1983. The Subcommittee reviewed the report and approved its submission to member plans as a "Medical Policy Newsletter." The newsletter provides information on the current status of NMR imaging as an investigational device, with a view toward clinical applications, technical considerations, and charges (18). The newsletter also offers advice to plans based on current evidence from the literature, from the FDA, and from the American College of Radiology. It is *not* intended, however, as a uniform medical policy statement, since the issue of NMR imaging is still under consideration by the Association.

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[6] Mobile Technology Inc., unpublished data, Los Angeles, CA, June 16, 1984.

Commercial Insurance Companies

Through December 1983, the HIAA had not received any inquiries from member organizations regarding NMR imaging (112). HIAA staff were also not aware of any claims for NMR services that might have been received by member companies. Therefore, the staff had not solicited an opinion on NMR imaging from the Council on Medical Specialty Societies.

According to a survey of 30 commercial companies that provide health insurance, by February 1984, five had determined that NMR was part of "generally accepted practice" and were paying for its use. In February, six other companies had acknowledged the clinical usefulness of NMR, but were reviewing each case before payment. By mid-June 1984, 10 of the 30 companies deemed NMR generally accepted and were paying for procedures, and 11 other companies had provisionally accepted NMR and were paying after review of each case.[7]

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[7] Ibid.

CONCLUSIONS

Since FDA has granted premarket approval to an NMR device, third-party payers now have major influence over the rate at which NMR imagers are acquired by hospitals. This influence derives not only from their decisions regarding whether to cover use of NMR, but also from their decisions regarding the circumstances in which use will be covered. Third-party payers such as HCFA, for example, will first need to decide whether they will reimburse for use of only those manufacturers' NMR devices that have gained PMA, or whether they will reimburse for use of any manufacturer's NMR device. Such a decision could have a major impact on the market share achieved by manufacturers in the short run.

Third-party payers will also have to decide whether to make a broad or narrow coverage decision. In the case of NMR, at least in the short run, this will come down to deciding whether to approve reimbursement for some applications of NMR imaging of the head only (the applications in which NMR has so far proved most efficacious), or whether to approve reimbursement for all uses of NMR, regardless of their stage of development. To the extent that the narrow strategy is followed, hospitals may be restrained in the speed with which they acquire NMR devices. To the extent that the latter strategy is followed, HCFA and other third-party payers will likely be subsidizing research on NMR applications that are less well developed.

The third major decision to be made by HCFA and other third-party payers is the monetary level at which outpatient use of the NMR imager will be reimbursed. How much of a difference in reimbursement is established for outpatient use of NMR as compared to outpatient use of X-ray CT will have a major impact on the rate at which NMR imaging systems diffuse into the outpatient setting. HCFA is beginning to pay hospitals prospectively on the basis of inpatient diagnosis, but will need to set an inpatient fee for physicians. Other third-party payers, such as Blue Cross and commercial insurers, may set inpatient rates, depending on their payment methods. Because it is likely that the outpatient rates set by HCFA will influence the inpatient rates established by Blue Cross and commercial insurers, HCFA's outpatient rate takes on even greater importance.

Another important decision to be made by third-party payers is the level at which professional fees for NMR imaging are set. At least in the near future, it can be expected that more professional time will be required for NMR scans than for X-ray CT scans. The level at which professional fees are established, therefore, may well have a significant impact on the level of interest that radiologists and other potential users manifest with regard to acquisition of NMR imaging devices.

Prospective systems of payment may have a major influence on the rate at which NMR diffuses throughout the medical system. With the introduction of DRG-based prospective payment under Medicare, hospitals will have to respond to different incentives from those to which they have been accustomed. Technology acquisition is one area of hospital operations in which change is likely to result. Hospitals, in theory, will have to weigh financial considerations against patient-care benefits more carefully when acquiring technologies. The constraints imposed by prospective payment on hospital budgets will likely deter some institutions from acquiring medical technologies that raise operating costs. In such instances, prospective payment may supersede State certificate-of-need regulation as a constraining influence on hospital investment decisions. In addition, hospitals may need to become more discriminating about deciding how acquired technology is used. Whether and how such rationing decisions will be made remain uncertain.

One potential concern about the advent of prospective systems of payment is whether some hospitals will be so financially constrained that they will be unable to acquire valuable new technology. If or when capital costs become included in the Medicare DRG payment rates, hospitals may be further constrained in their technology acquisition decisions. It is also important to realize that Medicare's DRG payment may vary among hospitals in its effect on their financial condition and their ability to acquire and use new technology. For some institutions, such as municipal hospitals serving large Medicare and Medicaid populations, the DRG payment system may exacerbate an already financially troubled state, impeding hospital capital formation necessary for the acquisition of high-cost but beneficial new technologies. The net effect may be to weaken further those institutions that are the primary sources of care for disadvantaged populations.

How much of an impact the prospective payment system will have on technology acquisition is likely to depend on HCFA decisions regarding updating and recalibration of DRG payment rates when new technologies become available (186). New technologies such as NMR are likely to be used across multiple DRGs. If NMR proves to be beneficial but not cost-saving in certain DRG applications, hospitals will be confronted by conflicting patient care and financial considerations. Periodic recalibration of DRG payment rates may thus be required as technological change in medicine occurs. In the absence of such recalibration, patients may be restricted from access to potentially beneficial new technologies.

9.

State Certificate-of-Need Programs

9.

State Certificate-of-Need Programs

INTRODUCTION

A major public policy response to the perceived problem of technology-induced cost inflation has been to attempt restraint of technology diffusion to hospitals (36). The prime policy instruments have been State certificate-of-need (CON) programs. CON programs vary considerably by State, but all essentially review and either approve or reject hospital equipment purchases involving technologies whose capital costs exceed some specified threshold or whose introduction to the hospital represents a significant change in service (36). NMR imaging devices, with anticipated sales prices of $800,000 to $2 million (see table 15 in ch. 5), are likely to come under the scrutiny of CON review in virtually every State. The potential impact of these programs and their policies on the adoption of NMR imagers is, therefore, of great interest.

This chapter is organized into four sections. The first section offers an overview of CON policies and strategies regarding the review of technology acquisition by hospitals and other providers. The second section describes the relationship of CON review to the FDA premarket approval process. Several important policy lessons drawn from the CON experience with CT scanning in the 1970s are discussed in the third section. The final section reviews the current status of CON activities that relate to NMR imaging devices.[1]

CERTIFICATE-OF-NEED POLICIES

Although CON programs were not originally intended to constrain the diffusion of medical technology (36), they have been used for that purpose.[2] To the extent that individual devices had price tags exceeding the established dollar threshold for CON review, new medical technologies became subject to CON regulation. As questions arose regarding the safety, efficacy, and costs associated with new technologies, a few CON programs set out to develop technology-specific resource and utilization standards for guiding the CON review process. The development of these standards and the evolution of CON policy toward medical technology proceeded, however, at a slow and nonuniform pace in most States (33). Complicating the problem was the fact that CON programs were being asked to control two interrelated, but distinct, aspects of technology diffusion (36): the *introduction* of new or innovative technology to the health care field, and the *distribution* of technology among individual health care institutions. Introduction, in this case, refers to the acceptance and adoption of innovation into clinical practice, whereas distribution implies the physical allocation of equipment among institutions (36).

Since the advent in 1976 of FDA regulation over market entry of new medical devices, the role of CON programs in controlling the "introduction" aspects of technology diffusion has diminished in importance, whereas its "distributive" role generally has been—and continues to be—its most

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[1] Readers interested solely in CON policies regarding NMR imagers may wish to read only the last section of this chapter.

[2] Certificate-of-need programs are State programs established by State legislation and governed by State rules and regulations. To be eligible to receive Federal funds for various health programs, each State CON program must meet Federal requirements, as prescribed in national health planning legislation (Public Law 93-641, 1974; Public Law 96-79, 1979), but effective control of the regulatory process resides with the individual State. The "section 1122 programs," named after a section of the Social Security Amendments of 1972 (Public Law 92-603), are also capital expenditure review programs sanctioned by the Federal Government. These programs are administered under contract by State governments, and are empowered to withhold portions of Medicare and Medicaid reimbursement for capital from institutions that incur large capital expenditures (including those for major medical equipment) without obtaining prior approval from a designated State health planning agency.

important quality. CON agencies frequently play pivotal roles in determining *which* institutions may acquire new technologies. Determinations based on broad concepts of "need," including the relative need demonstrated by competing CON applicants, are intended to ensure equitable allocation of new technology among hospitals. CON efforts to achieve distributional planning goals, however, have sometimes conflicted with program objectives involving cost containment. For example, as some observers (11) suggest, the misdirection of cost containment goals in the early years of X-ray CT scanner diffusion produced a maldistribution among hospitals that disenfranchised whole segments of the hospital industry—e.g., the municipal hospitals serving disadvantaged populations. Avoidance of this "franchising effect" is important if CON regulation is to have an even-handed impact on future diffusion of new technologies, such as NMR imaging devices.

In the past, CON programs have employed different policy orientations to address the issues associated with technology adoption and distribution (35,135). At various times, health planners have used strategies such as:

- *Pro forma denial*—denial of all CON applications for an indefinite period of time as a means of strict cost control; usually stems from serious concerns over the safety, efficacy, and cost of a technology.
- *Formalized strategy of delay*—temporary limitation of all CON applications, pending future availability of better data for CON review; often achieved through moratoria and application review deferrals.
- *Predetermined limits on diffusion*—limitation of CON approvals to specific sites or providers; often conditional on the provision of clinical data that can aid future evaluation of the technology.
- *Uncontested approval*—approval of CON applications for new technology in the absence of data on which to base sound CON decisions or in the face of statutory requirements that dictate approval unless need can be shown not to exist.

Of these four strategies, only the second and third have been used to advantage by CON agencies. All, however, suffer from their reliance on the high capital-cost "trigger" that is the hallmark of CON programs, and from their inability to review technologies in the premarket stages of development (36). For these reasons, CON programs have not been successful in either controlling the introduction of new technology or assuring equitable distribution of equipment among hospitals (135). A further problem is that CON review of innovative change places health planners on less familiar ground where they lack the requisite technical, medical, and analytic skills needed to answer important questions about safety and effectiveness in the absence of FDA findings (36). Newly emerging technologies are especially difficult to review since the information required for assessment is usually unavailable.

At present, State CON laws generally apply to the acquisition by hospitals of medical equipment and devices that exceed specified Federal dollar thresholds:[3] $400,000 for major medical equipment and $250,000 for new institutional services (Public Law 97-35, 1981). In order to receive Federal funds for various health programs, States must comply with Federal law that requires their CON statutes to contain provisions for review of acquisitions, by anyone, of major medical equipment that will be used to provide services to hospital inpatients (182). This requirement is intended to prevent circumvention of State CON laws either by hospitals that have been denied planning agency approval for a specific technology or by physician groups seeking to acquire and install major medical equipment in a facility outside the hospital (such as a medical arts building) where technology acquisitions may otherwise escape CON review. The precise coverage policies governing CON review vary by State program, but most do *not* cover equipment acquisition in physicians' offices. Only eight States (Colorado, Connecticut, Hawaii, Iowa, New Hampshire, Rhode Island, Virginia, and Wisconsin) plus the District of Columbia currently have CON laws that provide more stringent coverage of equipment acquisitions, such as in physicians' offices, than the minimum Federal requirements (182).

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[3] States must use these thresholds in order to comply with Federal law; they may, however, use more stringent thresholds, at their discretion.

RELATIONSHIP OF CON REVIEW TO THE FDA PREMARKET APPROVAL PROCESS

In theory, the FDA premarket approval process should precede the CON review process, but in practice, the two often coincide. In most States, "investigational devices" are exempt from full CON review, but a notice of intent to acquire such a device for research or experimental purposes must nevertheless be filed by the hospital with the appropriate health planning agency or agencies. Thus, a hospital may acquire an investigational device without passing through formal CON review while the device is undergoing FDA review for possible premarket approval. Once FDA approval is granted to a medical device, all subsequent acquisitions by other providers must undergo CON scrutiny, provided that the acquisition involves a setting (e.g., hospital, ambulatory care center, etc.) that is specifically *covered* by applicable State law. FDA premarket approval, therefore, is generally a prerequisite for widespread diffusion of a new technology but it does not necessarily guarantee broad adoption, since CON review is based on criteria that differ from those used by the FDA.

Whereas FDA review examines the safety and effectiveness of a medical device, CON review is concerned with demonstration of "need." The definition of "need" varies greatly by State CON program and may involve such diverse factors or criteria as: consistency of the proposed project with State health plans, consistency of the project with the institutional applicant's long-range plan, systemwide effects, financial feasibility of the project, access to care, quality of care, availability of services and personnel, construction and architectural considerations, effects on competition, competence and character of institutional management, and selection of the best alternative means of providing the proposed service (143). FDA assurance that a device is safe and effective is not sufficient to demonstrate need for the device.

The ability of some hospitals to acquire devices in the "investigational" stage of their development without having to undergo full CON review contains potential for abuse. As was the case with CT scanners—and as we are now seeing with NMR imagers—some hospitals tend to engage in "anticipatory behavior," i.e., they file applications for CON exemption early in the diffusion process in the hope of securing the technology before competition for the device leads to limited CON approvals. Once obtained, CON exemption bestows coveted status on a hospital relative to that of its competitors and establishes a "franchise" which, in practical terms, is not likely to be revoked by the CON program once FDA status of the device changes following premarket approval. Thus, the hospital that acquires NMR imaging as an investigational device is likely to keep the technology later when competing CON applications may be filed with the review agency. This "franchising effect" could, in the case of NMR imaging, work to the detriment of some segments of the hospital industry.

LESSONS FROM THE EXPERIENCE WITH X-RAY CT SCANNING

Several important lessons have emerged from the CON experience with X-ray CT scanning during the 1970s, the most important of which was that slowed technological diffusion has its advantages and disadvantages. In the case of X-ray CT scanning, early CON moratoria in some areas enabled health planners and hospitals to delay critical decisions pending further information. This delay tactic allowed society to "buy time" until better decisions regarding technology acquisition and "need" could be made. On the other hand, the inability of planners to evaluate the technology constrained its diffusion into medical practice more severely than may have been wise. The lack of available evaluative mechanisms and criteria for review made it difficult for planners to dispel the uncertainty surrounding X-ray CT scanning, thereby leading to many controversial and, at times, seemingly arbitrary decisions on individual CON applications. The net effect was a loss of credibility by the planners, as evidence of the truly revolutionary nature of X-ray CT scanning accumulated over time. The approach of selectively controlled diffusion now being used in some States (e.g., New York, Illinois, New Jersey) with regard to NMR imaging devices is more rational, by comparison (see next section).

A second and equally important lesson was that shared CT services among hospitals proved unsatisfactory for many institutions. Practical considerations, such as access and service volume needs, worked against the basic principles of sharing, causing many hospitals to abandon their shared-service arrangements and to acquire their own X-ray CT scanners. Moreover, some hospitals found that multiple X-ray CT units were required to meet service demand, making shared services even less enticing. The same potential problem exists for the shared-service arrangements now being proposed for NMR imaging in some areas of the country.

A third lesson involved the unusual behavior exhibited by hospitals in response to the incentives created by the CON process. Anticipatory behavior of the type described earlier was by no means unexpected. In some States, hospitals were able to acquire CT scanners before CON laws took effect. In other States, problems arose when CON programs failed to recognize the inherent inequities that were created by the nature of the process itself, i.e. hospitals that obtained investigational devices became "grandfathered" once diffusion of the technology accelerated and institutions that "played by the rules" were effectively penalized for not having taken action sooner. In addition, circumvention of CON authority occurred in many States where physicians' offices were not covered by State law. The ability of private radiology groups to make large capital purchases enabled these circumventions around the CON laws to succeed.

In the case of NMR imaging, it will be difficult to control these observed behaviors. A number of hospitals have already acquired NMR imagers at significant cost, including siting and construction costs for placement of the equipment. In practical terms, it will be extremely difficult for a health planning agency to dislodge an NMR unit from an existing site. Therefore, "franchising" has already begun and is likely to continue in some areas, at least in the near term. Without CON coverage of physicians' offices and other nonhospital settings, it will be virtually impossible to control the diffusion of NMR imagers to private groups who can raise the necessary capital. Thus, continued circumvention of CON regulation is equally likely to occur.

Finally, there is the lesson regarding the clinical utilization of X-ray CT scanning. Since its early diffusion, the clinical use of X-ray CT scanning has evolved and matured. Over the years, physicians have experimented with the technology, compared it with alternative modalities, and only now are beginning to understand its optimal application—i.e., when and how to use it as a diagnostic tool. NMR imaging is more complex and requires considerable expertise and skill on the part of the physician. It will be some time before the technology's optimal clinical application will be understood even among the experts. The next few years will be a period of clinical experimentation and learning, as physicians familiarize themselves with the technology and compare it to other diagnostic imaging modalities, including X-ray CT scanning. The potential impact of NMR imaging on the future practice of medicine may prove to be as far-reaching as was the case with X-ray CT scanning in the past decade. It may, thus, be appropriate to limit diffusion of the technology to selected sites—e.g., clinical research or teaching centers or a limited number of community hospitals, where evaluation of its proper place in clinical medicine may be conducted.

CON ACTIVITIES RELATED TO NMR IMAGING DEVICES

NMR imaging is emerging as an issue of great interest and concern to many Health Systems Agencies (HSAs) and State Health Planning and Development Agencies (SHPDAs). There are indications that these agencies, which hold responsibility for local and State CON review, respectively, are beginning to see increasing CON activity related to NMR imaging. Consequently, individual agencies in several States are taking aggressive action toward convening expert task forces, developing criteria and standards for CON review, and conducting reviews of CON applications already submitted by hospitals.

As a means of gathering information on CON activities involving NMR imaging, the National Health Planning Information Center (NHPIC) sent out "Program Information Letter 83-15" on July 8, 1983, to all health planning agencies requesting that they provide information on the number of actual proposals already reviewed, the number of anticipated reviews, criteria or guidelines for review of NMR imagers, and enacted or pending State legislation governing the placement of NMR units (194).

By mid-September 1983, 27 SHPDAs and 30 HSAs had responded to the NHPIC Program Information Letter, yielding a cross-sectional view of CON activities currently under way in many States (195). Program activities relating to NMR imaging fall into three main categories: applications review, criteria or standards development, and legislation or regulations adoption.

CON Reviews

As of September 12, 1983, 12 SHPDAs and 5 HSAs in the sample had conducted a total of 33 CON reviews for NMR imaging devices (195). SHPDAs reported review of 28 proposals with 16 approvals and HSAs reported 5 reviews with 3 approvals. The total of 19 approvals excludes waivers and exemptions for research applications. In addition, the agencies reported the receipt of 43 letters of intent or new proposals: 18 by SHPDAs and 25 by HSAs (195). Capsule summaries of selected CON reviews appear below.

Missouri

Missouri became the first State to approve NMR imaging in a nonresearch, nonuniversity-affiliated hospital setting when its CON agency, the Health Facilities Review Board, approved the applications of two community hospitals located in Columbia (64). The review board made these controversial decisions despite SHPDA recommendations to the contrary (64). The review board also rejected SHPDA recommendations for limited diffusion of NMR imaging to only university hospital settings and for the formation of a task force to develop criteria and standards for CON review of the technology (99).

The two hospitals receiving CON approval are Columbia Regional Hospital, a 301-bed facility that is part of the Lifemark investor-owned hospital chain, and Boone Hospital Center, a county-owned, nonprofit facility with 344 beds (64).

Illinois

In the absence of NMR criteria for CON review, the Illinois CON agency (the Health Facilities Planning Board) has invoked the technologically innovative equipment clause of the State CON law to *limit* the diffusion of NMR imaging to medical school affiliated hospitals (see later discussion under legislation or regulations). As of August 1983, two hospitals affiliated with medical schools (Rush-Presbyterian-St. Luke's Medical Center in Chicago, and St. Francis' Hospital in Peoria) had applied for and received CON approval for NMR imaging devices (72).

Nebraska

Beginning in late 1982 and early 1983, the State CON agency received multiple applications for NMR from individual hospitals in Omaha. In an effort to encourage cooperative planning, the State agency announced in the spring of 1983 that it would "batch" NMR applications for simultaneous review (205). Three private, nonprofit hospitals (Nebraska Methodist, Archbishop Bergan Mercy, and Children's Hospitals) responded by forming a private corporation, NMR Inc., which submitted a single CON application to place an NMR imager in a freestanding facility where all three hospitals would share access. In July 1983, NMR Inc. received CON approval for the acquisition of a superconducting NMR system. Also receiving CON approval in July for NMR imaging was the University of Nebraska Hospital, which has referral agreements with two other facilities, Omaha Veterans' Hospital and Bishop Clarkson Hospital (205). One other CON application for NMR was reviewed and recommended for denial; the hospital subsequently withdrew the application and is now seeking a cooperative arrangement with a second hospital (205).

Kentucky

Albert B. Chandler Hospital, a teaching affiliate of the University of Kentucky, currently has an NMR imaging unit, which was granted exemption from CON review as a research/experimental device (62). In May 1983, the State CON agency reviewed and disapproved an application for NMR from Audubon Hospital, a Louisville facility that is part of the Humana investor-owned hospital chain. In making its decision, the SHPDA invoked the Kentucky State Health Plan, signed by the Governor, which states that NMR technology ". . . shall be considered a tertiary level service and approval of one unit will be considered for each of the two designated tertiary centers"[4] in the State (195). The CON decision was appealed by the hospital and granted reconsideration by the SHPDA (62). Since Humana leases and manages the tertiary center in Louisville (Humana Hospital-University), the corporation argued that placement of an NMR imager at Audubon Hospital (a Humana-owned facility) would still permit patients from the university hospital to have access to the technology. Following a public hearing, Audubon Hospital's application was approved by the SHPDA.

The University of Kentucky's Albert B. Chandler Hospital has applied for CON approval to use its previously installed NMR unit for clinical, as well as research, purposes.

Other jurisdictions in which CON applications for NMR have been reviewed include: SHPDAs in Georgia, Tennessee, Texas, Ohio, Iowa, Arizona, Kansas, and California; and HSAs in Middle Tennessee, New York City, North Central Georgia, Chicago, and Southeast Kansas.

CON Criteria or Standards Development

As of September 12, 1983, 10 health planning agencies (HSAs and SHPDAs) had reported to the National Health Planning Information Center that they had established NMR-specific review criteria or guidelines. An additional 15 agencies are in the process of developing review criteria (195). Two of these reported that they were using CON review criteria or standards for CT scanners as the basis for their efforts in NMR imaging (158). Several agencies have also formed or are beginning to form expert task forces or advisory panels. A brief summary of current State and local efforts in this regard appears below.

Nebraska

The Statewide Health Coordinating Council (SHCC) in April 1983 authorized the formation of a 12-member Task Force on New Developments in Diagnostic Radiology to develop NMR guidelines. The Task Force consists of seven radiologists, one internist, one neurosurgeon, and one consumer member of the SHCC (205). In September 1983, the Task Force submitted for review a set of draft guidelines for NMR scanners. The SHCC also created a separate Task Force on New Technological Developments, which prepared and submitted in September 1983 draft guidelines for review of emerging technologies.

Massachusetts

The SHPDA in Massachusetts is working with the State CON agency (the Determination of Need program) to develop criteria and guidelines for CON review of NMR (28). An Advisory Committee on NMR is being formed, with representatives drawn from the State Rate Setting Commission the hospital industry, the professional medical societies, and consumers. It is anticipated that the State may move toward limited diffusion of NMR imaging during an initial research/experimentation phase (28).

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[4] "Centers" refers to the two university hospitals in the state: Albert B. Chandler Hospital in Lexington and Humana Hospital-University in Louisville (62).

In an apparently independent effort, the Health Planning Council for Greater Boston (the State's largest HSA) developed proposed guidelines for NMR, which were expected to be adopted in final form in December 1983 (79). The proposed guidelines would allow NMR units to be placed in clinical, nonteaching settings under certain conditions (79).

Georgia

The Georgia SHPDA, with the aid of medical specialty societies and other professional groups, has convened a "blue ribbon committee" of experts to develop NMR-specific criteria and guidelines for review (75). The committee, which is composed of radiologists, nuclear medicine specialists, internists, and hospital administrators, was expected to release a draft final report in the fall of 1983. The anticipated recommendations are likely to urge caution, with NMR diffusion temporarily restricted to two medical schools pending FDA approval and the articulation of reimbursement policies for NMR (75).

Oklahoma

The State CON agency in Oklahoma is now in the process of assembling a Select Committee on Technology to recommend criteria and standards for NMR (25). Two avenues that will likely be explored are the limited diffusion strategy of the Illinois CON program and the group application/shared-service model encouraged by the Nebraska CON program (see the earlier discussions of both States' experiences with CON reviews).

In addition to these CON programs, other agencies involved in either task force development or criteria/standards development include SHPDAs in the District of Columbia, New Jersey, North Carolina, Illinois, Ohio, Maryland, Hawaii, Florida, and Pennsylvania, and HSAs in Southeastern Massachusetts, Central New Jersey, Eastern Virginia, North Central Georgia, Western Michigan, Central Arizona, and Northwest Oregon (69,134,172,195). Several other agencies have developed either NMR plans (Newark HSA, Southeast Kansas HSA) or position papers (Southeastern Pennsylvania HSA, Southwestern Pennsylvania HSA). Developmental activities of this nature are expected to continue and expand in other areas of the Nation (13).

The American College of Radiology (ACR), a medical specialty society, has been contacted by many State CON agencies requesting information on NMR imaging. In response to these requests, the ACR (through its Commission on NMR, Subcommittee on Government Relations) prepared a document, "Guidelines for Preparation of CON Applications," intended to assist State CON agencies in performing reviews of NMR-related CON applications.

State CON Legislation/Regulations

During 1983, significant developments occurred in several States regarding CON legislation or regulations that affect the review of NMR imaging devices. A sampling of major developments follows.

New York

The New York State Hospital Review and Planning Council, the CON body in the State, drafted regulations that call for a 2-year demonstration period in which NMR imaging will be restricted to a select number of hospitals (127). During this period, data on the technology's safety, efficacy, and cost effectiveness will be gathered and analyzed. Upon completion of the demonstration, a determination of need will be made and, provided that neither cost effectiveness nor quality of care is at issue, all participants in the demonstration as well as any other hospitals in the State may then apply for CON approval. The proposed regulations were expected to be reviewed and approved by the council in the fall of 1983. The council made the decision in April 1984 to permit placement of NMR imagers in no more than 13 teaching hospitals during the demonstration period (19).

The application for NMR submitted by New York Hospital is generally credited with having precipitated this regulatory process (127). The hospital's application was approved with the understanding that it could not receive reimbursement for NMR unless it was selected to participate in the planned demonstration. The Major Medical Equipment Committee of the Council will commence development of NMR review criteria or standards once the demonstration gets under way and preliminary data are produced.

Illinois

As alluded to earlier in the discussion of CON reviews, the Illinois Department of Public Health and the Illinois Health Facilities Planning Board adopted regulations on March 1, 1983, that set forth specific "Standards and Criteria for Review of Applications for Permit for Technologically Innovative Equipment or Innovative Programs" (195). These regulations stipulate that any such equipment or programs must be restricted to only medical school settings until FDA premarket approval for the technology is granted and CON guidelines or criteria for review have been established. This effectively limits NMR diffusion to only 11 hospitals in the State (one hospital per medical school). NMR imaging is among the first technologies to be regulated under these rules (72).

District of Columbia

In September 1982, the CON law in the District of Columbia was amended to permit the designated CON agency the right to declare a 180-day "holding period" on the review of any new technology whose safety, efficacy, and clinical use are not clearly understood or are in question (134). The CON agency has, since that time, drafted general criteria and standards for CON review. Two clauses specifically relate to new technology. One requires that applicants demonstrate to the SHPDA director's satisfaction that the technology is beneficial in controlled trials. The second clause requires applicants to demonstrate need for technology acquisition relative to actual or potential need for such technology at other institutions in the District. The agency received a CON application for NMR imaging from an area hospital in February 1984 and immediately invoked the 180-day moratorium provision pending development of review criteria (203). The agency has convened a techical advisory panel and expected to develop criteria and standards for review of NMR imagers by August 1984.

New Jersey

In November 1983, the New Jersey SHCC approved a proposal that would restrict CON approval of NMR imagers to no more than four sites over an evaluation period of 2 years (69). In selecting the four sites, preference will be given to the State's 16 major teaching hospitals. Data gathered from the four installations would be used to guide decisionmaking on future NMR diffusion in New Jersey. In an unprecedented move, the State Commissioner of Health asserted that these new NMR regulations would apply to physicians' offices as well as other health care facilities (69). Under present New Jersey law, physicians in private practice are exempt from CON review (195). However, the State Department of Health views the purchase of NMR by physicians' groups as going "far beyond the private practice of medicine" (69).

Utah

The CON law in Utah was amended in May 1983 to *exempt* all medical equipment from CON review (74). NMR imaging devices, therefore, will not be subject to CON review in Utah, as the State appears to be pursuing a strategy of uncontested approval for all medical equipment purchases.

California

The State of California has also passed legislation that eliminates the dollar thresholds for CON review of major medical equipment purchases (201). As in Utah, NMR imaging devices will not be subject to CON review in California.

Future Prospects

The general consensus among health planners and CON agency staff members who were contacted for this study was that the level of CON activity related to NMR imaging is likely to increase dramatically over the next year. Once HCFA renders a policy decision regarding Medicare coverage, planners expect to see a rapid increase in the number of CON applications filed by hospitals around the Nation.[5] In anticipation of this onslaught of paperwork, CON agencies at both State and local levels in the national health planning structure are continuing to push forward in the creation of special task forces and in the development of criteria and standards for CON review.

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[5] Several proposals are now before the Congress that would raise the CON thresholds for equipment review to $1 million or higher. If such legislation was enacted in the next few months, some States might follow suit and amend their statutes, effectively exempting the less expensive NMR systems from CON review.

Of the four strategies previously described for CON treatment of medical technologies, at least three appear to be operating with respect to NMR imaging. The New York, Illinois, Ohio, Kentucky, and New Jersey SHPDAs; and the Eastern Virginia HSA all appear to be employing predetermined limits on diffusion, whereas the Southeast Kansas HSA and the District of Columbia SHPDA have adopted moratoria on NMR pending further study and planning (38,69,117,195). Nebraska, by contrast, is encouraging shared-service arrangements. Both Utah and California, at this time, appear to be using a strategy of uncontested approval. No CON program, on the other hand, has adopted a policy of pro forma denial.

NMR imaging is likely to differ from the CT experience in several ways. First, and foremost, are the site considerations that are unique to NMR imaging. Unlike the placement of CT scanners, NMR installation is costly and is likely to have considerable impact both on hospital plant configuration and on the organization of staff. NMR placement can be disruptive to the hospital, making internal management of the technology and its use far more difficult than was (or is) the case with CT. Shared service arrangements among hospitals may prove fragile, owing to the fact that host institutions may experience difficulty in rationing the use of NMR imaging among participants. Utilization of NMR units may increase tremendously as physicians discover new clinical applications and perform "sequential scanning." Should NMR imaging come to be used in this way, hospital administrators will find it difficult to ration NMR use among medical staff members, let alone among other hospitals. Interspecialty disputes over the use of NMR imaging may further cloud the issues of appropriate utilization and rationing.

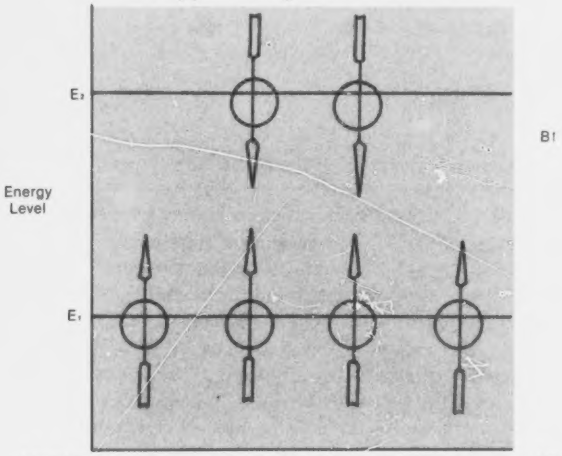
Appendixes

Appendix A.—NMR: Technical Background

NMR Spectroscopy—Technical Background

Ordinarily the magnetic moments of hydrogen atoms (the vector representations of the net magnetic properties of hydrogen atoms) will point in random directions.[1] When exposed to an externally applied magnetic field, however, these magnetic moments tend to align themselves either parallel to or antiparallel to the magnetic field.[2] Because the energy state of a hydrogen nucleus is lower when its magnetic moment is pointing in the direction of the applied magnetic field than when it is pointing in the opposite direction, more of the magnetic moments will point in the direction of the applied field than in the opposite direction. In quantum mechanical terms, hydrogen nuclei exposed to an externally applied magnetic field, B, will reside in one of two possible magnetic energy levels (see fig. A-1). For hydrogen nuclei to go from the lower energy level, E_1, to the higher energy level, E_2, an $E_2 - E_1$ amount of energy needs to be added to the system. When hydrogen nuclei go from the higher energy level to the lower energy level, in contrast, $E_2 - E_1$ energy is emitted from the system.

Figure A-1.—Energy Levels of Hydrogen Atoms in Applied Magnetic Fields



SOURCE: E. P. Steinberg, Johns Hopkins Medical Institutions, Baltimore, MD, 1983.

According to quantum theory, hydrogen nuclei will move from E_1 to E_2 *only* when *exactly* the right amount of energy (namely $E_2 - E_1$) is applied to the system. In NMR experiments, excitational energy is provided in the form of radiofrequency (RF) waves. In order for hydrogen nuclei residing in energy level E_1 to be excited into level E_2 by such radiofrequency energy, the RF waves must be applied at exactly the same rotational frequency as that at which the magnetic nuclei in E_1 are precessing.[3] This frequency is known as the Larmor frequency.

When an NMR system is appropriately constructed (see fig. A-2), the energy emitted by excited hydrogen nuclei during the process of relaxation can be detected as an NMR signal. The intensity of the signal will be proportional to the number of hydrogen nuclei in the sample being studied.

Variations in the local magnetic field give rise to variations in the frequency at which nuclei spin. These spin differences depend on the exact molecular environment in which each nucleus exists. This observed "shift" in nuclear precessional frequency, and therefore the radiofrequency at which NMR signals are detected, has been termed "chemical shift." These slight variations in NMR signals induced by variations in molecular environment provide the basis for NMR spectroscopy and its use in acquisition of information about molecular structure and conformation.

Application of NMR Principles to Imaging—Technical Background

A decade ago, scientists realized that exciting possibilities emerged if, instead of applying a *uniform* magnetic field across an experimental sample, they established a magnetic field *gradient* across it (see fig. A-3). In so doing, the strength of the magnetic field, B, varies from one line (L_1) to another (L_2). Because of the one-to-one relationship between the magnetic field strength in which magnetic nuclei exist and the frequency of radiofrequency energy that will excite them, a pulse of radiofrequency energy applied to the system depicted in figure A-3 will be absorbed (and subsequently re-emitted) only by nuclei that are located in the vertical line L_x of magnetic field strength B_x that corresponds to the Larmor frequency of the energy being applied. By sequentially varying the frequency of the energy being supplied, one can thus selectively excite nuclei, line by line. The establishment of a magnetic field gradient across a sample thus "spa-

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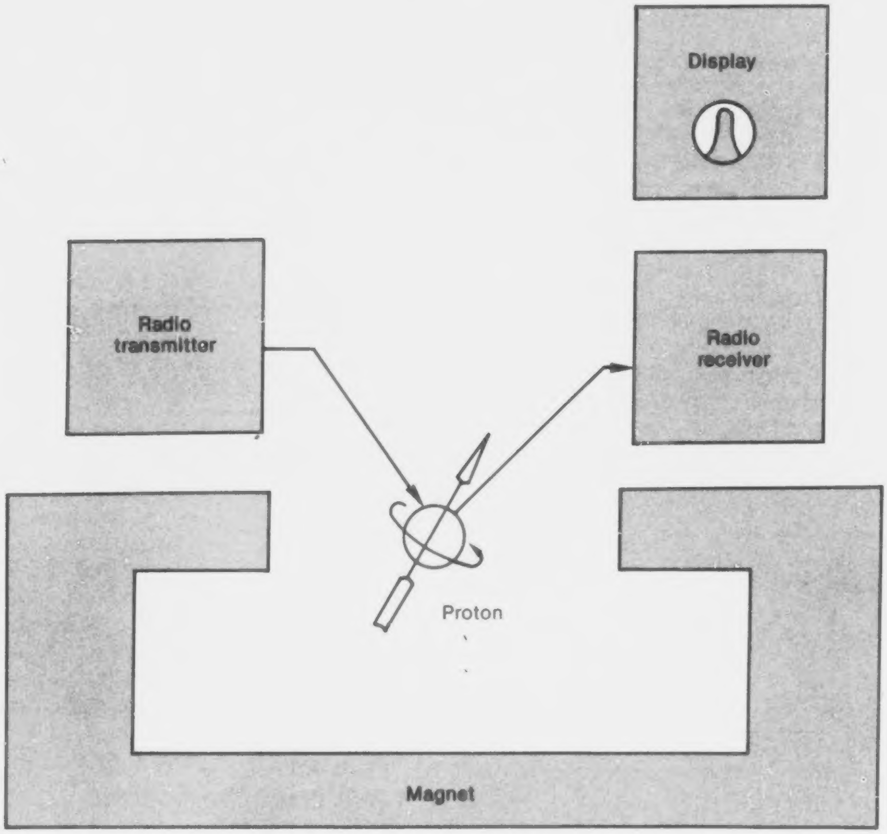
[1] For simplicity, the remainder of this discussion will pertain to hydrogen, which has a spin of one-half (a quantum nuclear spin number of one-half to describe the rotation of the hydrogen nucleus).

[2] Other forces, such as thermal agitation, will influence the orientation of these magnetic moments, but consideration of such forces is beyond the scope of this case study.

[3] Precession is a term describing the motion of a proton in an external magnetic field or of a top in the Earth's gravitational field.

Figure A-2.—Schematic Diagram of NMR System



The radiotransmitter provides radiowaves at the appropriate rotational frequency to excite the proton. When the radiowaves are turned off, the excited protons precess in phase, thereby producing radiowaves that are detected with a radio receiver and then displayed.

SOURCE: E. P. Steinberg, Johns Hopkins Medical Institutions, Baltimore, MD, 1983.

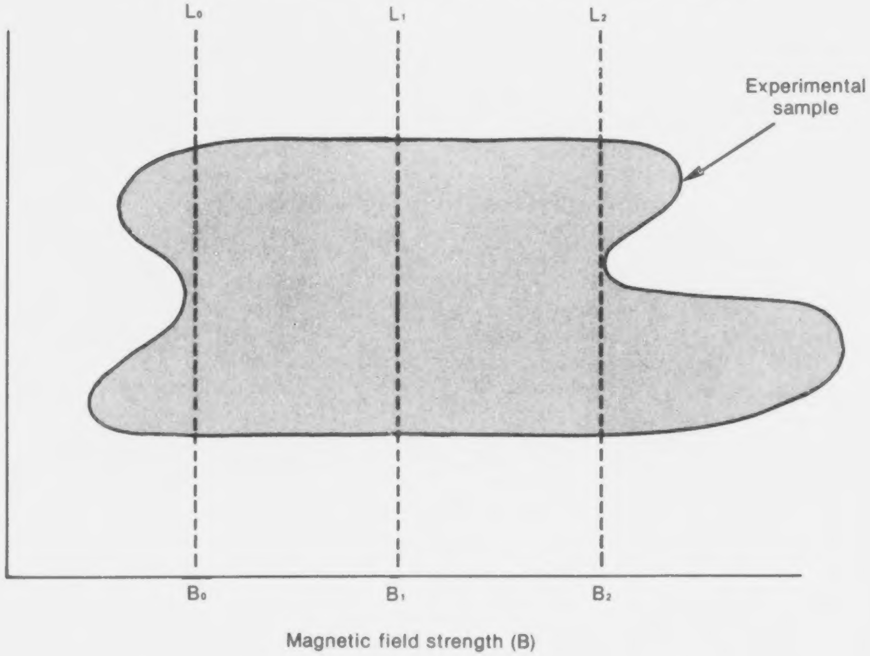
tially encodes" the NMR information inherent in a system. This type of spatial encoding of the origin of a NMR signal forms the basis of NMR imaging.

Radiofrequency Pulse Sequences

As explained earlier, NMR signals are obtained through the excitation of magnetic nuclei with RF waves. In a typical NMR experiment, the nuclei to be excited (and imaged) are repeatedly exposed to RF waves in a pulsed fashion. Specific "pulse sequences" are characterized by the duration and intensity of each pulse used, as well as by the interval between repeated pulses.

Several different types of pulse sequences can be utilized to produce NMR images. Probably the three most common types of sequences currently employed in NMR imaging are Saturation Recovery, Inversion Recovery, and Spin-Echo sequences (27,55,77). Although the exact technical details of how these sequences are produced are beyond the scope of this report, it should be mentioned that Saturation Recovery and Inversion Recovery sequences result in NMR signals (and therefore images) that tend to reflect

Figure A-3.—Experimental Sample in Magnetic Field Gradient



(Magnetic field strength in line L_0 is B_0; in line L_1 is B_1; and in line L_2 is B_2.)

SOURCE: E. P. Steinberg, Johns Hopkins Medical Institutions, Baltimore, MD, 1983.

predominantly the T_1 character of tissues (i.e., they are T_1 weighted), whereas Spin-Echo sequences tend to reflect more T_2 information (i.e., they are T_2 weighted). NMR images will thus vary depending upon the particular pulse sequences used to produce them. Considerable effort is being expended on trying to define pulse sequences that optimally demonstrate different types of morphologic and pathologic abnormalities. This task is formidable, given the infinite number of pulse sequences that can be used.

Techniques for Spatial Encoding and Image Acquisition

Several different techniques have been developed through which NMR information can be spatially encoded, acquired, and transformed into an image. The first such technique, adapted from use in X-ray computed tomography (CT) reconstructions, was the projection-reconstruction method of NMR imaging used by Lauterbur (115). In this technique, magnetic gradients are electronically rotated to produce multiple projections of the sample being imaged. These projections are then "pieced together" with the help of a computer to construct an NMR image. Imaging methods developed subsequently employ a variety of techniques to "selectively excite" nuclei. These techniques have acquired names based on whether they excite nuclei on a point-by-point (sequential point methods), line-by-line (sequential line methods), plane-by-plane (planar imaging) or whole-volume (three-dimensional imaging) basis (8). The latter techniques require less time to form images (8). The recently developed echo-planar method of imaging permits scans to be obtained in milliseconds, raising the possibility of dynamic, or real-time, NMR imaging (133).

Appendix B.—Survey of Manufacturers: Methods

To gather the information required for this report, a survey of NMR-imaging-device manufacturers was conducted involving the following steps:

1. With the assistance of the National Electrical Manufacturer's Association (NEMA), appropriate contacts (either the director of marketing or the technical director for NMR imaging) were identified in each of the firms represented by NEMA. Potential contact persons in non-NEMA companies were identified through other sources. A total of 20 companies were targeted for survey.
2. Letters of introduction describing the study and its purpose were mailed to all identified manufacturers in June 1983. Manufacturers were notified of our intent to contact them by telephone to arrange a mutually convenient time for a telephone interview.
3. Between June and August, 15 manufacturers were interviewed. Interviews varied in length, but the average discussion lasted approximately 1 to 1½ hours. In each case, the discussion was structured around the following key issues:
   - History of the firm's program in NMR imaging—its genesis and development to the present day
   - Current status of the manufacturer's NMR imaging systems—including magnet type, magnet field strength, and imaging capabilities
   - Clinical placements of NMR imaging systems—by site, system capabilities, and date of installation
   - Collaborative relationships with universities and/or medical schools for NMR-imaging R&D
   - Company characteristics—size, ownership, staff composition, and product lines
   - The future market for NMR imaging systems—projected growth, competitive technologies (e.g., CT, ultrasound, etc.), and key factors influencing NMR diffusion
   - Costs of NMR-imaging devices—likely capital acquisition costs, annual operating expenses once installed
   - FDA policies—premarket approval for Class III devices
   - Third party payment policies—HCFA/Medicare coverage decisions, Blue Cross/Blue Shield decisions, commercial insurers' decisions, prospective payment systems
   - State certificate-of-need policies
   - Federal role in funding applied R&D
   - Patents
   - Future plans for NMR-imaging development
4. Follow-up telephone calls were made for clarification of responses, as necessary.
5. Upon submission of the draft final report to OTA in early September, each of the 15 participating manufacturers was invited by OTA to review and comment on its respective company description contained in appendix C to this report. In addition, representatives of NEMA were invited by OTA to review the full draft report.

Appendix C.—Manufacturers of NMR Imaging Devices

The following company descriptions of NMR-imaging-device manufacturers are based on interviews with representatives from each firm. The initial interviews took place in 1983 and information was updated in August 1984. Magnet field strength is stated in kilogauss (kG). Conversion of kilogauss to Tesla units is as follows: 10kG = 1.0T.

ADAC LABORATORIES
4747 Hellyer Avenue
San Jose, CA 95138

Background: ADAC Laboratories is an independent publicly owned company. The company decided to invest in R&D efforts for NMR in 1982. ADAC is in the early stages of NMR-imaging-system development. It expects to have an engineering model available in early 1986 and a commercial prototype system in the second half of 1986.

Current NMR-imaging models: None (permanent magnet prototype is in development)
Collaborative arrangements with universities or medical centers: Negotiated, yet to be announced.
Clinical placement sites: None
Number of employees engaged in NMR imaging: 40 (including magnet developers)
Other diagnostic imaging products: Nuclear medicine, digital radiography; conventional X-ray; and fluoroscopy
Other medical products: Radiation-therapy planning; special procedures room; clinical information systems; medical linear accelerators
Non-health-care-related products: Instruments for nondestructive testing

BRUKER MEDICAL INSTRUMENTS, INC.
Manning Park
Billerica, MA 01821
(Head Office: West Germany)

Background: Bruker Instruments is a privately owned subsidiary of Bruker A.M. of West Germany. The company began work on NMR spectroscopy in 1961 and developed extensive magnet technology and experience with pulse and spectroscopy techniques. Bruker made its first commitment to NMR imaging in 1977, and by 1979, had completed its first experimental prototypes. In 1982, Bruker placed its first NMR-imaging unit in an outside clinical setting. In 1983, the company acquired Oxford Research Systems, which specializes in animal research systems, from Oxford Instruments and plans to build superconducting magnets with its new subsidiary. Bruker had its first marketing prototype available for placement in 1983.

Current NMR-imaging models:

Magnet type	Field strength	Bore size	Year first available
Resistive	1.3 kG	Whole body	1979
Superconducting	47 kG	Animal	1979
Superconducting	19 kG	Animal or head only	1982
Resistive (self-shielded)	2.4 kG	Whole body	1984

Collaborative arrangements with universities or medical centers: 2
1. Baylor College of Medicine, Houston, TX
2. Yale University, New Haven, CT

Clinical placement sites:

Hospital or clinic	NMR imaging system	Date of installation (E = expected)
1. Baylor College of Medicine, Houston, TX	Resistive, 1.3 kG, whole body	1982
2. Baylor College of Medicine, Houston, TX	Superconducting, 47 kG, animal	1982
3. Japan	Resistive, 1.3 kG, whole body	1982

4. Brigham & Women's Hospital, Boston	Resistive, 1.3 kG, whole body	1983
5. Brigham & Women's Hospital, Boston	Superconducting, 19 kG, animal	1983
6. D.K.D. Hospital, Wiesbaden, West Germany	Resistive, 1.3 kG, whole body	1983
7. Yale University, New Haven, CT	Superconducting, 15 kG, whole body	1985E

Number of employees engaged in NMR imaging: 50
Other diagnostic imaging products: None
Other medical products: Parent firm makes ECG monitors, mobile defibrillators, and patient monitoring systems
Non-health-care-related products: NMR spectrometers

CGR MEDICAL CORP.
2519 Wilkins Avenue
Baltimore, MD 21203
(Head office: Paris, France)

Background: CGR Medical Corp. is a private, wholly owned subsidiary of Thompson-Brandt of France. The company was created in 1971 by the acquisition of Westinghouse Medical X-Ray Division by CGR of France, which merged in 1979 with Thompson-CSF to form Thompson-Brandt. CGR Medical Corp. decided to invest in R&D efforts for NMR imaging in 1979. Its first engineering models were available in 1982. The company expects to place its first NMR imaging unit in a clinical setting and to have available for placement its first commercial system in 1984.

Current NMR-imaging models:

Magnet type	Field strength	Bore size	Year first available
Resistive	1.5 kG	Whole body	1982
Superconducting	3.5 kG	Whole body	1983
Superconducting	5 kG	Whole body	1983

Collaborative arrangements with universities or medical centers: None in USA (number in Europe not available)
Clinical placement sites: None
Number of employees engaged in NMR imaging: approximately 150
Other diagnostic imaging products: Computed tomography; ultrasonography; nuclear medicine; digital radiography; conventional X-ray and fluoroscopy
Other medical products: None
Non-health-care-related products: Parent firm makes assorted electrical appliances and equipment

DIASONICS INC.
NMR Division
533 Cabot Road
South San Francisco, CA 94080

Background: Diasonics is an independent, publicly owned company. Initial R&D on NMR imaging began in 1975 as a University of California, San Francisco (UCSF) project with outside funding. In 1976 Pfizer Corp. began funding the work. In 1981, Diasonics purchased the rights to all patentable NMR technology developed under the UCSF-Pfizer agreement. Diasonics had its engineering model available in 1981, and the company made its first clinical placement of an NMR imaging unit the same year. Its first commercial prototype system became available for placement in 1983.

Current NMR-imaging models:

Magnet type	Field strength	Bore size	Year first available
Superconducting	5 kG[a]	Whole body	1981

[a] System operating at 3.5 kilogauss; probable commercial prototype system; commitment to upgrade to higher fields if Diasonics believes clinical relevance demonstrated.

Collaborative arrangements with universities or medical centers: 3

1. University of California, San Francisco
2. University of Texas, Dallas
3. University of Michigan, Ann Arbor

Clinical placement sites:

Hospital or clinic	NMR imaging system	Date of installation (E = expected)
1. University of California, San Francisco	Superconducting, 5 kG, whole body	1981
2. Huntington Medical Research Institutes, Pasadena, CA	Superconducting, 5 kG, whole body	April 1983
3. University of Texas Health Science Center, Dallas	Superconducting, 5 kG, whole body	September 1983
4. Private radiology clinic, NJ	Superconducting, 5 kG, whole body	1983
5. University of Michigan, Ann Arbor	Superconducting, 5 kG, whole body	1983
6. St. Anthony's Professional Building St. Petersburg, FL	Superconducting, 5 kG, whole body	1984
7. UCSF-Radiation Instrumentation Laboratory, San Francisco, CA	Superconducting, 20 kG, whole body	1984
8. Montclair Radiological Association, PA, Montclair, NJ	Superconducting, 5 kG, whole body	1983
9. University of Texas Health Science Center, Dallas	Superconducting, 20 kG, whole body	1984
10. NMR Associates, Houston, TX	Superconducting, 5 kG, whole body	1984
11. Private clinic, Wuppertal, West Germany	Superconducting, 5 kG, whole body	1984
12. Institute of Radiology, Geneva, Switzerland	Superconducting, 5 kG, whole body	1984
13. Roentgen Institut, Dusseldorf, West Germany	Superconducting, 5 kG, whole body	1984
14. NMR Imaging, Torrance, CA	Superconducting, 5 kG, whole body	1984
15. Long Island MRI, New Hyde Park, NY	Superconducting, 5 kG, whole body	1984
16. Northeast Medical Center, Ft. Lauderdale, FL	Superconducting, 5 kG, whole body	1984
17. Magnetic Resonance Images, Inc., St. Petersburg, FL	Superconducting, 5 kG, whole body	1984
18. Diagnostic Imaging Center, Lausanne, Switzerland	Superconducting, 5 kG, whole body	1984
19. Heart to Heart, Phoenix, AZ	Superconducting, 5 kG, whole body	1984
20. San Jose MRI, San Jose, CA	Superconducting, 5 kG, whole body	1984

21. NMR Scan Center, Ft. Lauderdale, FL	Superconducting, 5 kG, whole body	1984
22. NMR Imaging, Santa Ana, CA	Superconducting, 5 kG, whole body	1984
23. Magnetic Resonance Center of San Diego, San Diego, CA	Superconducting, 5 kG, whole body	1984

Number of employees engaged in NMR imaging: 152
Other diagnostic imaging products: Ultrasonography and surgical C-arm imaging equipment
Other medical products: None
Non-health-care-related products: None

ELSCINT LTD.

Head Office: Haifa, Israel
U.S. Subsidiary: Elscint Inc.
930 Commonwealth Avenue
Boston, MA 02215

Background: Elscint is an independent, publicly owned company in Israel. The company decided to invest in R&D efforts for NMR imaging in 1981, and by 1982, had developed its first engineering model. Elscint produced its first prototype NMR imaging system in 1983 and expects to have a second prototype in late 1984. The company made its first clinical placement outside the company's plant in November 1983.

Current NMR-imaging models:

Magnet type	Field strength	Bore size	Year first available
Superconducting	5 kG	Whole body	1982

Collaborative arrangements with universities or medical centers: 2
1. Hebrew University, Jerusalem, Israel
2. Weitzman Institute, Rehovoth, Israel

Clinical placement sites:

Hospital or clinic	NMR Imaging system	Date of installation (E = expected)
1. Skokie Valley Imaging, Skokie, IL	Superconducting, 5 kG, whole body	1983
2. Fondren Imaging, Houston, TX	Superconducting, 5 kG, whole body	1984
3. Private clinic, Freiburg, West Germany	Superconducting, 5 kG, whole body	1984
4. Herzlyia MRI Clinic, Herzlyia, Israel	Superconducting, 5 kG, whole body	1983

Number of employees engaged in NMR imaging: Not available
Other diagnostic imaging products: Computed tomography; ultrasonography; nuclear medicine; digital radiography; conventional X-ray; and fluoroscopy
Other medical products: None
Non-health-care-related products: None

FONAR CORP.

110 Marcus Drive
Melville, NY 11747

Background: Fonar has been an independent, publicly owned corporation since 1981. Founded originally as the RAANEX Corp., it has invested in R&D efforts for NMR imaging since 1978. In 1980, Fonar completed its first experimental prototype and made its first clinical placement of a unit outside the plant. The firm's first commercial prototype system became available for placement in 1983.

Current NMR-imaging models:

Magnet type	Field strength	Bore size	Year first available
Permanent	0.4 kG	Whole body	1980
Permanent	3 kG[a]	Whole body	1983
Permanent	3 kG[a]	Whole body (mobile)	1983

[a] Probable commercial prototype system(s).

Collaborative arrangements with universities or medical centers: 1

1. University of California at Los Angeles (UCLA)

Clinical placement sites:

	Hospital or clinic	NMR imaging system	Date of installation (E = expected)
1.	Diagnostic Imaging Associates, Cleveland, OH	Permanent, 0.4 kG, whole body	December 1980 (This unit is no longer in place)
2.	Hospital Universitario, Monterey, Nuevo Leon, Mexico	Permanent, 0.4 kG, whole body	April 1981
3.	San Raffaele Hospital, Milan, Italy	Permanent, 0.4 kG, whole body	March 1982
4.	Nakatsugawa Hospital, Nagoya, Japan	Permanent, 0.4 kG, whole body	July 1982
5.	Brunswick Memorial Hospital, Amityville, NY	Permanent, 3 kG, whole body	October 1983
6.	Universal NMR, Inc. (mobile scanner)	Permanent, 3 kG, whole body	October 1983
7.	UCLA	Permanent, 3 kG, whole body	1984
8.	Montvale Diagnostic Imaging Center, Montvale, NJ	Permanent, 3 kG, whole body	1984
9.	Neurodiagnostic Center, New York, NY	Permanent, 3 kG, whole body	1984E
10.	Chicago Medical School, Chicago, IL	Permanent, 3 kG, whole body	1984
11.	NMR Centers, Inc., Los Angeles, CA	Permanent, 3 kG, whole body	1984E
12.	Parkview Hospital, Nashville, TN (Hospital Corporation of America)	Permanent, 3 kG, whole body	1984E
13.	Loyola University, Chicago, IL	Not available	Not available
14.	Mercy Hospital, Altoona, PA	Permanent, 3 kG, whole body	1984E
15.	AMD (Advanced Medical Diagnostics), Melbourne, FL	Permanent, 3 kG, whole body	1984E
16.	NMR Investors, Inc., Santa Monica, CA	Permanent, 3 kG, whole body	1984E
17.	Odessa Diagnostic Imaging Center, Odessa, TX	Permanent, 3 kG, whole body	1984E

Number of employees engaged in NMR imaging: 100
Other diagnostic imaging products: None
Other medical products: None
Non-health-care-related products: None

GENERAL ELECTRIC CO.

Medical Systems Business Group
P. O. Box 414
3000 Grandview Avenue
Milwaukee, WI 53201

Background: General Electric is a publicly owned, multiproduct company. The Medical Systems Business Group is responsible for NMR imaging R&D. Early R&D work in phosphorus spectroscopy began in 1978, but firm corporate commitment to NMR imaging was not made until 1980. In 1982, General Electric completed its first engineering model and made its first clinical placement of an NMR imaging unit outside the company's plant. General Electric expects to have its first commercial prototype available for placement in late 1984.

Current NMR-imaging models:

Magnet type	Field strength	Bore size	Year first available (E = expected)
Superconducting	15 kG[a]	Whole body	1984E

[a] Probable commercial prototype.

Collaborative arrangements with universities or medical centers: 4

1. University of Pennsylvania, Philadelphia, PA
2. Medical College of Wisconsin, Milwaukee, WI
3. Yale University, New Haven, CT
4. Duke University, Durham, NC

Clinical placement sites:

Hospital or clinic	NMR imaging system	Date of installation (E = expected)
1. University of Pennsylvania Hospital, Philadelphia, PA	Resistive, 1.2 kG, whole body	October 1982
2. Yale University School of Medicine, New Haven, CT	Resistive, 1.5 kG, whole body	August 1983
3. Duke University, Durham, NC	Superconducting, 15 kG, whole body	February 1984
4. Memorial Sloan Kettering Cancer Center, New York, NY	Superconducting, 15 kG, whole body	August 1985E
5. Medical College of Wisconsin, Milwaukee, WI	Superconducting, 15 kG, whole body	October 1984E
6. Pittsburgh NMR Institute, Pittsburgh, PA	Superconducting, 15 kG, whole body	November 1984E
7. University of Illinois, Chicago, IL	Superconducting, 15 kG, whole body	February 1984E
8. University of Nebraska, Omaha, NE	Superconducting, 15 kG, whole body	April 1985E
9. Henry Ford Hospital, Detroit, MI	Superconducting, 15 kG, whole body	January 1985E
10. Ohio State University, Columbus, OH	Superconducting, 15 kG, whole body	November 1984E
11. Michigan State University, Ann Arbor, MI	Superconducting, 15 kG, whole body	February 1985E
12. New York Hospital—Cornell University, New York, NY	Superconducting, 15 kG, whole body	December 1984E
13. Rochester Consortium, Rochester, NY	Superconducting, 15 kG, whole body	November 1984E

14. State University of New York at Albany Medical School, Albany, NY	Superconducting, 15 kG, whole body	March 1985E
15. University of Texas Health Science Center, San Antonio, TX	Superconducting, 15 kG, whole body	March 1985E
16. University of Texas/Herman Hospital, Houston, TX	Superconducting, 15 kG, whole body	March 1985E
17. Driscoll Children's Hospital, Corpus Christi, TX	Superconducting, 15 kG, whole body	March 1985E
18. University of Washington, Seattle, WA	Superconducting, 15 kG, whole body	December 1984E
19. Stanford University, Palo Alto, CA	Superconducting, 15 kG, whole body	December 1984E
20. University of Western Ontario, London, Ontario, Canada	Superconducting, 15 kG, whole body	February 1985E

Number of employees engaged in NMR imaging: in excess of 500

Other diagnostic imaging products: Computed tomography, ultrasonography, nuclear medicine, digital radiography, conventional X-ray, and fluoroscopy

Other medical products: Assorted electromedical equipment

Non-health-care-related products: Assorted electrical appliances and equipment

JEOL USA, INC.

235 Birchwood Avenue
Cranford, NJ 07016
(Head office: Japan)

Background: JEOL USA is a publicly owned subsidiary of JEOL of Japan. JEOL has been manufacturing NMR spectrometers since 1960. In 1973, the parent firm was acquired by Mitsubishi. In 1982, the firm began investing in NMR imaging and spectrometry R&D. JEOL has decided not to pursue the clinical NMR market, and will instead focus on the research and experimentation market. The firm expects to have its first engineering model available in 1984.

Current NMR-imaging models: None

Collaborative arrangements with universities or medical centers: None

Clinical placement sites: None

Number of employees engaged in NMR imaging: 5

Other diagnostic imaging products: None

Other medical products: Radioimmunoassay equipment, blood gas analyzers; fluid analyzers

Non-health-care-related products: NMR spectrometers. Parent firm also makes electron microscopes.

M&D TECHNOLOGY LTD.*

Unit 1, Whitemyres Avenue
Aberdeen, Scotland, U.S. AB2-6HQ

Background: M&D Technology is an independent, private company in Scotland. M&D was formed in 1982 to commercially develop the NMR imaging system that had evolved from the work of Professor Mallard at Aberdeen, Scotland since 1974. M&D's first engineering model became available in 1982. In 1983 the company made its first clinical placement of a NMR imaging unit. Also, for a short time during 1983, M&D had entered into a marketing agreement with Fischer Imaging Corporation. M&D expected to have a marketing prototype system availabble in 1984.

Current NMR-imaging models:

Magnet type	Field strength	Bore size	Year first available
Resistive	0.4 kG	Whole body	197?
Resistive	0.8 kG	Whole body	1982

Collaborative arrangements with universities or medical centers: 1

1. University of Aberdeen, Scotland, U.K.

Clinical placement sites:

Hospital or clinic	NMR imaging system	Date of installation (E = expected)
1. Edinburgh Royal Infirmary, Edinburgh, U.K.	Resistive, 0.8 kG, whole body	1983
2. Private Clinic, Geneva	Resistive, 0.8 kG, whole body	1983
3. Two additional sites		End of 1983E

Number of employees engaged in NMR imaging: Not available
Other diagnostic imaging products: None
Other medical products: None
Non-health-care-related products: None

*Information on M&D Technology Ltd. is as of October 1983.

NALORAC CRYOGENICS CORP.
1717 Solano Way, Suite #37
Concord, CA 94520

Background: Nalorac Cryogenics is an independent, privately owned company, which was founded in 1975 by Dr. James Carolan to develop and manufacture superconducting magnets, cryogenic devices, and NMR systems. In 1977, the company was acquired by Nicolet Instrument Corp. In 1981, Dr. Carolan purchased the company back from Nicolet and reaffirmed its commitment to developing NMR-imaging magnets and systems. The company currently manufactures superconducting high resolution NMR magnet systems with bore diameters from 50 to 320 mm. and field strengths from 20 kG to 70 kG. The company is presently developing a complete imaging spectrometer system which is scheduled for introduction in early 1985.

Projected NMR-imaging models (spectrometer systems):

Magnet type	Field strength	Bore size	Year first available
Superconducting	20-40 kG	Animal (330 mm)	1985E
Superconducting	20 kG	Pediatric (450 mm)	1986E
Superconducting	10 kG	Head/appendage (600 mm)	1987E

Collaborative arrangements with universities or medical centers: No formal arrangements will be announced prior to late 1984.

Clinical placement sites:

Hospital or clinic	NMR imaging system	Date of installation (E = expected)
1. University of California, San Francisco	Superconducting, 60 kG, 100 mm bore	January 1984
2. University of Texas Health Science Center, Houston, TX	Superconducting, 20 kG, 320 mm bore	June 1984

Number of employees engaged in NMR imaging: 10
Other diagnostic imaging products: None
Other medical products: None
Non-health-care-related products: Superconducting high resolution analytical NMR magnets, gradient coils, power supplies, dewars, NMR probeheads

PHILIPS MEDICAL SYSTEMS, INC.

710 Bridgeport Avenue
Shelton, CT 06484
(Head Office: The Netherlands)

Background: Philips Medical Systems is a subsidiary of North American Philips. Approximately 61 percent of the common stock of North American Philips is owned by Connecticut National Bank as trustee of the United States Philips Trust. Through the trust, North American Philips has strong relationships with N.V. Philips and their Medical Systems Division in Eindhoven, the Netherlands. In 1977, the company made a firm commitment to invest in NMR-imaging research. In 1981, their first engineering model was completed and used to image patients in the Netherlands. In 1983, Philips installed a 15 kG whole-body system in a U.S. medical center; the system is being used to image hydrogen and sodium. Philips is presently manufacturing three NMR models for worldwide distribution. Philips has been working with both Oxford and IGC (Intermagnetics General Corp.) to obtain superconducting magnets. The company had commercial prototype systems available for placement in 1983.

Current NMR-imaging models:

Magnet type	Field strength	Bore size	Year first available
Resistive	1.5 kG[a]	Whole body	1982
Superconducting	30 kG	Animal	1982
Superconducting	15 kG[a b]	Whole body	1983
Superconducting	5 kG[a b]	Whole body	1983

[a] For sale as a product in the rest of the world.
[b] Investigational status in the United States only.

Collaborative arrangements with universities or medical centers: 2

1. Neurological Institute, Columbia-Presbyterian Hospital, New York, NY
2. University of Leiden, Leiden, The Netherlands

Clinical placement sites:

Hospital or clinic	NMR imaging system	Date of installation (E = expected)
1. Neurological Institute Columbia-Presbyterian Hospital, New York, NY	Superconducting, 30 kG, animal	1982
2. Neurological Institute Columbia-Presbyterian Hospital, New York, NY	Superconducting, 15 kG, whole body	1983
3. University of Leiden, The Netherlands	Resistive, 1.5 kG, whole body	1983
4. Columbia-Presbyterian Hospital, New York, NY	Superconducting, 5 kG, whole body	1985E
5. Emory University, Atlanta, GA	Superconducting, 15 kG, whole body	1984E
6. New York University/Bellevue Hospital, New York, NY	Superconducting, 5 kG, whole body	1984E
7. Northwestern University Hospital, Chicago, IL	Superconducting, 15 kG, whole body	1984E
8. Akademisch Ziekenhuis Leiden, Leiden, The Netherlands	Resistive, 1.5 kG, whole body	August 1983
9. Casa di cura "Pio X," Milano, Italy	Resistive, 1.5 kG, whole body	September 1983
10. Instituto Neurotraumatologico Italiano, Rome, Italy	Resistive, 1.5 kG, whole body	April 1984
11. Universitá di Firenze, Florence, Italy	Superconducting, 5 kG, whole body	September 1984E

12. Casa di cura "Pio X," Milano, Italy	Superconducting, 5 kG, whole body	September 1984E
13. Erasmus Ziekenhuis/Free University, Brussels, Belgium	Superconducting, 15 kG, whole body	October 1984E
14. Universitaetsklinik Koeln Cologne, West Germany	Superconducting, 5 kG, whole body	October 1984E
15. Akademisch Ziekenhuis Leiden, Leiden, The Netherlands	Superconducting, 5 kG, whole body	November 1984E
16. Neuro Besta, Milano, Italy	Resistive, 1.5 kG, whole body	November 1984E
17. Montreal Neurological Institute, Montreal, Canada	Superconducting, 15 kG, whole body	December 1984E
18. Centro Diagnostico Immagini Computerizzate, Catania, Italy	Superconducting, 5 kG, whole body	December 1984E

Number of employees engaged in NMR imaging: 30—North American Philips (U.S.); 80—N.V. Philips (The Netherlands)

Other diagnostic imaging products: Computed tomography; ultrasonography; digital radiography; conventional X-ray and fluoroscopy; nuclear medicine[c]

Other medical products: Assorted electromedical equipment. Parent firm also produces surgical supplies and dental equipment

Non-health-care-related products: NMR spectrometers. Parent company produces assorted electrical appliances and equipment

[c] Nuclear medicine imaging products distributed by ADAC in the United States and by N.V. Philips in the rest of the world.

PICKER INTERNATIONAL, INC.

595 Miner Road
Highland Heights, OH 44143
(Head office: United Kingdom)
(Corporate headquarters: Ohio)

Background: Picker International is a U.S. corporation operating as an 80-percent-owned subsidiary of the General Electric Company (P.L.C.) of England (GEC). The company was formed in April 1981 through the acquisition of Picker from RCA in combination with GEC Medical and Cambridge Medical Instruments. GEC had earlier acquired the NMR technology of EMI of England and, by the end of 1981, the first Picker International NMR unit was clinically operating. In 1983, the first commercial units were shipped.

Current NMR-imaging models:

Magnet type	Field Strength	Bore size	Year first available
Resistive	1.5 kG[a]	Whole body	1978
Superconducting	3 kG	Whole body	1981
Superconducting	5 kG[a]	Whole body	1983

[a] Probable commercial prototype.

Collaborative arrangements with universities or medical centers: 11

1. University of Nottingham, Nottingham, U.K.
2. Royal Postgraduate Medical School and Hammersmith Hospital, London, U.K.
3. Mount Sinai Hospital, Cleveland, OH
4. Mayo Clinic, Rochester, MN
5. Bowman Gray Medical School, Winston-Salem, NC
6. University of British Columbia, Vancouver, Canada
7. City of Faith Medical and Research Center, Tulsa, OK
8. National Institutes of Health, Bethesda, MD
9. University of Iowa, Iowa City, IA
10. Queens Square Hospital, London, U.K.
11. National Heart Institute, London, U.K.

Clinical placement sites:

	Hospital or clinic	NMR imaging system	Date of installation (E = expected)
1.	University of Nottingham Hospital, Nottingham, U.K.	Resistive, 1.5 kG, whole body	1978
2.	HIRST Research Center, London, U.K.	Resistive, 1.5 kG, whole body	November 1978
3.	Queens Medical Center, Nottingham, U.K.	Resistive, 1.5 kG, whole body	February 1981
4.	Hammersmith Hospital, London, U.K.	Superconducting, 3.5 kG, whole body (operating at 1.5 kG)	March 1981
5.	Mount Sinai Hospital, Cleveland, OH	Resistive, 1.5 kG, whole body	October 1982
6.	Mayo Clinic, Rochester, MN	Resistive, 1.5 kG, whole body	December 1982
7.	University of British Columbia, Vancouver, British Columbia, Canada	Superconducting, 3 kG, whole body	March 1983
8.	University of Manchester, Manchester, U.K.	Superconducting, 3 kG, whole body	March 1983
9.	Bowman Gray Medical School, Winston-Salem, NC	Resistive, 1.5 kG, whole body	June 1983
10.	Dr. Wallnhofer, Private Clinic, 6500 Mainz 1, Munich, West Germany	Superconducting, 3 kG, whole body	July 1983
11.	Dr. Assheuer, Private Clinic, 500 Koln 80, Cologne, West Germany	Superconducting, 3 kG, whole body	October 1983
12.	City of Faith Medical and Research Center, Tulsa, OK	Superconducting, 5 kG, whole body	1983
13.	National Institutes of Health (NIH), Bethesda, MD	Superconducting, 5 kG, whole body	1983
14.	University of Alabama, Birmingham, AL	Superconducting, 5 kG, whole body	1984E
15.	Duarte CT, Duarte, CA	Superconducting, 5 kG, whole body	1984
16.	Neurology Center, Washington, DC	Superconducting, 5 kG, whole body	1984
17.	University of Iowa, Iowa City, IA	Superconducting, 5 kG, whole body	1984
18.	Queens Square Hospital, London, U.K.	Superconducting, 5 kG, whole body	1984
19.	National Heart Institute, London, U.K.	Superconducting, 5 kG, whole body	1984
20.	Private clinic, Cologne, West Germany	Superconducting, 5 kG, whole body	1984
21.	Private clinic, Frankfurt, West Germany	Superconducting, 5 kG, whole body	1984
22.	Chiba University, Chiba City, Japan	Superconducting, 5 kG, whole body	1984
23.	First Hill Diagnostic, Seattle, WA	Resistive, 1.5 kG, whole body	1984
24.	Glasgow Hospital, Glasgow, Scotland	Resistive, 1.5 kG, whole body	1984
25.	Shinsuma University, Cobe, Japan	Resistive, 1.5 kG, whole body	1984
26.	Picker Clinical Research Center, Cleveland, Ohio	Resistive, 1.5 kG, whole body	1984
27.	Picker Clinical Research Center, Cleveland, OH	Superconducting, 5 kG, whole body	1984

28. Picker Clinical Research Center, Cleveland, OH	Superconducting, 15 kG, whole body	1984
29. HIRST Research Center, London, U.K.	Superconducting, 20 kG, whole body	1984

Number of employees engaged in NMR imaging: 410

Other diagnostic imaging products: Computed tomography; ultrasonography; nuclear medicine; digital radiography; conventional X-ray; and fluoroscopy

Other medical products: Electrocardiogram equipment. Parent company makes other electromedical equipment

Non-health-care-related products: None

SIEMENS MEDICAL SYSTEMS, INC.

186 Wood Avenue South
Iselin, NJ 08830
(Head office: West Germany)

Background: Siemens Medical Systems is a publicly owned subsidiary of Siemens A.G. of West Germany. As early as 1965, Siemens had a research group in NMR working on blood flow and blood viscosity. In 1978, the company made a commitment to develop NMR-imaging systems. The first engineering model was put into operation in 1980. A year later, Siemens made its first clinical placement of an NMR-imaging unit outside the company's plant. The company had a commercial prototype system available for placement in 1983.

Current NMR-imaging models:

Magnet type	Field strength	Bore size	Year first available
Resistive	1.2 kG	Whole body	1980
Resistive	2 kG	Whole body	1981
Superconducting	5 kG[a]	Whole body	1983
Superconducting	15 kG[a]	Whole body	1983

[a] Probable commercial prototypes.

Collaborative arrangements with universities or medical centers: 6

1. Washington University, St. Louis, MO
2. University of Hanover Medical Center, Hanover, West Germany
3. Radiological Institute, Frankfurt, West Germany
4. Radiological Institute, Munich, West Germany
5. Mount Sinai Medical Center, Miami, FL
6. Allegheny General Hospital, Pittsburgh, PA

Clinical placement sites:

Hospital or clinic	NMR imaging system	Date of installation (E = expected)
1. University of Hanover Medical Center, Hanover, West Germany	Resistive, 2 kG, whole body	1982
2. Radiological Institute, Munich, West Germany (Dr. Heller)	Superconducting, 5 kG, whole body	June 1983
3. Mallinckrodt Institute, Washington University, St. Louis, MO	Superconducting, 5 kG, whole body	July 1983
4. Radiological Institute, Frankfurt, West Germany (Dr. Kuehnert)	Superconducting, 5 kG, whole body	September 1983
5. Allegheny General Hospital, Pittsburgh, PA	Superconducting, 5 kG, whole body	October 1983

6. Mount Sinai Medical Center, Miami FL	Superconducting, 5 kG, whole body	November 1983
7. Mallinckrodt Institute, Washington University, St. Louis, MO	Superconducting, 20 kG, whole body	May 1984
8. St. Vincent Medical Center, Los Angeles, CA	Superconducting, 5 kG, whole body	April 1984
9. Pomona Valley Community Hospital, Pomona, CA	Superconducting, 15 kg, whole body	1984E
10. Loma Linda University Medical Center, Loma Linda, CA	Superconducting, 15 kG, whole body	1984E
11. Memorial Hospital Medical Center of Long Beach, Long Beach, CA	Superconducting, 15 kG, whole body	April 1984
12. Hershey Medical Center, Hershey, PA	Superconducting, 15 kG, whole body	NA
13. Boone County Medical Center, Columbia, MO	Superconducting, 5 kG, whole body	April 1984
14. Radiology Associates, Little Rock, AR	Superconducting, 10 kG, whole body	May 1984
15. St. Francis Medical Center, Peoria, IL	Superconducting, 5 kG, whole body	1984E
16. Digital Diagnostics, Baton Rouge, LA	Superconducting, 15 kG, whole body	1984E
17. Magnetic Resonance Imaging, Inc., Brooklyn, NY	Superconducting, 15 kG, whole body	1984E
18. Wendover Park Associates, Greensboro, NC	Superconducting, 10 kG, whole body	1984E
19. University of Minnesota, Minneapolis, MN	Superconducting, 10 kG, whole body	1984E
20. Ochsner Foundation, New Orleans, LA	Superconducting, 20 kG, whole body	1984E
21. University of Virginia, Charlottesville, VA	Superconducting, 10 kG, whole body	1984E
22. American Shared Hospital Services, San Francisco, CA	Superconducting, 15 kG, whole body	April 1984
23. Pacific Medical Center, San Francisco, CA	Superconducting, 10 kG, whole body	1984E
24. Siemens Headquarters, Iselin, NJ	Superconducting, 20 kG, whole body	March 1984
25. Flower Hospital, Toledo, OH	Superconducting, 10 kG, whole body	1984E
26. Magnetic Imaging Associates, Los Angeles, CA	Superconducting, 15 kG, whole body	1984E
27. Southwest Texas Methodist Hospital, San Antonio, TX	Superconducting, 15 kG, whole body	1984E
28. University Diagnostic Institute of Tampa, Tampa, FL	Superconducting, 10 kG, whole body	1984E
29. American Shared Services, San Francisco, CA	Superconducting, 10 kG, whole body	five systems expected in 1984-85
30. Florida Medical Association, Tampa, FL	Superconducting, 10 kG, whole body	1984E
31. Medical College of Virginia, Richmond, VA	Superconducting, 10 kG, whole body	1984E

32. Magnetic Resonance, Inc., Rockville, MD	Superconducting, 10 kG, whole body	1984E
33. Magnetic Resonance of Williamsport, Williamsport, VA	Superconducting, 15 kG, whole body	1984E
34. Mid Miami Assets MRI, Miami, FL	Superconducting, 15 kG, whole body	1984E
35. Harper Hospital, Detroit, MI	Superconducting, 15 kG, whole body	1984E
36. Faculty Medical Practice, Memphis, TN	Superconducting, 20 kG, whole body	1984E
37. New England Medical Center, Boston, MA	Superconducting, 10 kG, whole body	1984E
38. Long Island Jewish Hospital, New Hyde Park, NY	Superconducting, 20 kG, whole body	1984E
39. Methodist Hospital, Houston, TX	Superconducting, 5 kG, whole body	1984E
40. Nebraska Methodist Hospital, Omaha, NE	Superconducting, 15 kG, whole body	1984E
41. Mount Sinai Medical Center, Miami, FL	Superconducting, 15 kG, whole body	1984E
42. Methodist Hospital, Houston, TX	Superconducting, 20 kG, whole body	1984E
43. Fox Chase Medical Center, Philadelphia, PA	Superconducting, 20 kG, whole body	1984E
44. Private clinic, New York, NY	Superconducting, 10 kG, whole body	1984E
45. New Rochelle Radiology, New Rochelle, NY	Superconducting, 5 kG, whole body	1984E
46. Private clinic, Munich, West Germany	Superconducting, 5 kG, whole body	1984
47. University of Berlin, Berlin, West Germany	Superconducting, 5 kG, whole body	1984
48. University of Hiedelberg, Heidelberg, West Germany	Superconducting, 5 kG, whole body	1984
49. University of Hiedelberg, Heidelberg, West Germany	Superconducting, 15 kG, whole body	1984
50. University of Upsala, Upsala, Sweden	Superconducting, 5 kG, whole body	1984
51. University of Tokyo, Tokyo, Japan	Superconducting, 5 kG, whole body	1984

Number of employees engaged in NMR imaging: 100

Other diagnostic imaging products: Computed tomography; ultrasonography; nuclear medicine; digital radiography; conventional X-ray; and fluoroscopy

Other medical products: Assorted electromedical equipment

Non-health-care-related products: Parent company produces assorted electrical appliances and equipment

TECHNICARE CORP.
29100 Aurora Road
Solon, OH 44139

Background: Technicare is a publicly owned subsidiary of Johnson & Johnson. Johnson & Johnson made an initial commitment to NMR imaging as early as 1977, but major R&D effort did not begin until the acquisition of Technicare in 1979 from Ohio Nuclear. In 1980, the company completed its first engineering model. The following year Technicare made its first clinical placement of an NMR-imaging system. In 1982, the Magnet Corporation of America was acquired to build superconducting magnets for Technicare's NMR-imaging systems. That same year, Technicare had its first commercial prototype available for placement.

Current NMR-imaging models:

Magnet type	Field strength	Bore size	Year first available
Superconducting	15 kG[a]	Animal	1980
Resistive	1.5 kG[a]	Head only	1981
Superconducting	3 kG[b]	Whole body	1982
Superconducting	5 kG[a]	Whole body	1983
Superconducting	6 kG	Whole body	1983
Superconducting	15 kG	Whole body	1983

[a] Probable commercial prototype system(s).
[b] No longer available.

Collaborative arrangements with universities or medical centers: 17

1. Massachusetts General Hospital, Boston, MA
2. University Hospital, Cleveland, OH
3. Cleveland Clinic Foundation, Cleveland, OH
4. University of Kentucky, Lexington, KY
5. Indiana University, Indianapolis, IN
6. Hershey Medical Center, Hershey, PA
7. Millard Fillmore Hospital, Buffalo, NY
8. St. Joseph's Hospital, London, Ontario, Canada
9. Johns Hopkins University, Baltimore, MD
10. Ontario Cancer Institute, Toronto, Canada
11. Charlotte Memorial Hospital, Charlotte, NC
12. New York Hospital, New York, NY
13. Vanderbilt University, Nashville, TN
14. Defalquu Clinic, Charleroi, Belgium
15. University of Florida, Gainesville, FL
16. Baylor University Medical Center, Dallas, TX
17. Rush Presbyterian-St. Luke's Medical Center, Chicago, IL

Clinical placement sites:

Hospital or clinic	NMR imaging system	Date of installation (E = expected)
1. Massachusetts General Hospital, Boston, MA	Superconducting, 15 kG, animal	1981
2. Massachusetts General Hospital, Boston, MA	Resistive, 1.5 kG, head only	1981
3. University Hospital, Cleveland, OH	Superconducting, 3.0 kG, whole body	October 1982
4. Cleveland Clinic Foundation, Cleveland, OH	Resistive, 1.5 kG, whole body	November 1982
5. University of Kentucky, Lexington, KY	Resistive, 1.5 kG, whole body	December 1982

6. Indiana University, Indianapolis, IN	Resistive, 1.5 kG, whole body	February 1983
7. Hershey Medical Center, Hershey, PA	Resistive, 1.5 kG, whole body	February 1983
8. Millard Fillmore Hospital, Buffalo, NY	Resistive, 1.5 kG, whole body	March 1983
9. St. Joseph's Hospital, London, Ontario, Canada	Resistive, 1.5 kG, whole body	March 1983
10. Ontario Cancer Institute, Toronto, Canada	Resistive, 1.5 kG, whole body	March 1983
11. New York Hospital, New York, NY	Superconducting, 5 kG, whole body	June 1983
12. Charlotte Memorial Hospital, Charlotte, NC	Resistive, 1.5 kG, whole body	February 1983
13. Defalque Clinic, Charleroi, Belgium	Resistive, 1.5 kG, whole body	April 1983
14. Vanderbilt University, Nashville, TN	Superconducting, 5 kG, whole body	July 1983
15. Shands Teaching Hospital, University of Florida, Gainesville, FL	Resistive, 1.5 kG, whole body	October 1983
16. Houston Imaging Center, Houston, TX	Superconducting, 3 kG, whole body	July 1983
17. Cleveland Clinic Foundation, Cleveland, OH	Superconducting, 6 kG, whole body	August 1983
18. Cleveland Clinic Foundation, Cleveland, OH	Superconducting, 15 kG, whole body	May 1984
19. Massachusetts General Hospital, Boston, MA	Superconducting, 6 kG, whole body	February 1984
20. Scottsdale Memorial Hospital, Scottsdale, AZ	Superconducting, 6 kG, whole body	September 1983
21. AMC Cancer Research Center and Hospital, Lakewood, CO	Resistive, 1.5 kG, whole body	June 1983
22. St. Luke's Hospital, Jacksonville, FL	Resistive, 1.5 kG, whole body	December 1983
23. Rush Presbyterian-St. Luke's Medical Center, Chicago, IL	Superconducting, 5 kG, whole body	November 1983
24. Greenberg Radiology Clinic, Highland Park, IL	Resistive, 1.5 kG, whole body	June 1983
25. North Shore University Hospital, Manhasset, NY	Superconducting, 6 kG, whole body	December 1983
26. University Park Imaging, Urbana, IL	Superconducting, 6 kG, whole body	June 1984
27. Veterans Administration Medical Center, St. Louis, MO	Resistive, 1.5 kG, whole body	February 1984
28. NMR SA, Barcelona, Spain	Resistive, 1.5 kG, whole body	January 1984
29. ML and Associates, New York, NY	Resistive, 1.5 kG, whole body	October 1983
30. University Hospitals of Cleveland/ Case Western Reserve University, Cleveland, OH	Superconducting, 15 kG, whole body	July 1984
31. Baylor University Medical Center, Dallas, TX	Superconducting, 6 kG, whole body	January 1984
32. Temple Radiology, New Haven, CT	Resistive, 1.5 kG, whole body	February 1984
33. Albert Einstein Medical Center, Philadelphia, PA	Resistive, 1.5 kG, whole body	March 1984
34. Nuclear Facilities, Brooklyn, NY	Superconducting, 5 kG, whole body	May 1984

35. NMR Diagnostic Center, Sun City, AZ	Resistive, 1.5 kG, whole body	January 1984
36. Garden State Medical Center, Marlton, NJ	Superconducting, 6 kG, whole body	June 1984
37. Magnetic Imaging of Bellville, Bellville, IL	Superconducting, 6 kG, whole body	March 1984
38. Private clinic, Union, NJ	Superconducting, 6 kG, whole body	August 1984
39. Ft. Worth Magnetic Imaging Institute, Ft. Worth, TX	Superconducting, 5 kG, whole body	August 1984
40. Broward NMR, Ft. Lauderdale, FL	Superconducting, 5 kG, whole body	January 1984
41. Clairval Hospital, Marseille, France	Resistive, 1.5 kG, whole body	December 1983
42. Private clinic, Hanover, West Germany	Superconducting, 5 kG, whole body	November 1983
43. Clinique du Park, Paris, France	Resistive, 1.5 kG, whole body	April 1984
44. Private clinic, Antwerp, Belgium	Resistive, 1.5 kG, whole body	April 1984

Number of employees engaged in NMR imaging: 100

Other diagnostic imaging products: Computed tomography; ultrasonography; nuclear medicine; digital radiography

Other medical products: Parent firm makes surgical instruments and supplies; dental equipment

Non-health-care-related products: None

Appendix D.—Glossary of Terms and Acronyms

Glossary of Terms

Field strength: The strength of the magnetic field of a magnet.

Inhomogeneities in magnetic field: Lack of uniformity in magnetic field strength.

Ionizing radiation: A form of radiant energy within the electromagnetic spectrum that has the capability of penetrating solid objects and altering the electrical charge of their atoms. High-energy radiation, such as X-rays and gamma rays, is ionizing radiation.

Kilogauss: A unit of measurement of the magnetic force per unit area that can be generated within a defined region. (See *tesla*.)

Magnetic field gradient: A magnetic field that increases or decreases in strength in a given direction along a sample.

Magnetic moments: The vector representations of the net magnetic properties of hydrogen atoms.

Medical technology: The drugs, devices, medical and surgical procedures used in medical care, and the organizational and supportive systems within which such care is provided.

Nuclear: Pertaining to the nucleus, the positively charged central portion of an atom that consists of protons and neutrons, except in hydrogen, which has only one proton.

Paramagnetic: A substance with a small but positive magnetic susceptibility (magnetizability) that may increase the contrast between tissues and NMR images (4).

Prospective payment: Payment for medical care according to rates set in advance of the period during which they apply.

Pulse sequence: The pattern of radiofrequency energy used to excite protons.

Radiation: Emission of or exposure to radiant energy, which travels as a wave motion. Radiant energy ranges from low-frequency, nonionizing radiofrequency waves used in NMR to high-frequency, ionizing waves used in X-rays.

Radiofrequency waves: Low-energy, electromagnetic waves that do not emit ionizing radiation and that are used in NMR imaging.

Rate of loss of coherence: The rate at which protons stop rotating in phase with each other.

Relaxation time characteristics: The rate at which tissue hydrogen atoms that have been excited by radiofrequency energy return to their equilibrium states.

Resonance: The oscillation of nuclei between higher and lower energy levels as radiofrequency energy is applied and withdrawn.

Shimming: Adjustments, such as addition of special coils, made to eliminate inhomogeneities in the magnetic field.

Spatial resolution: The extent to which two adjacent structures can be distinguished.

Spectrogram: Graphic depiction of the individual components of NMR signals from phosphorus-containing compounds arranged according to frequency.

Spectroscopy: A technique in which the individual components of the NMR signals from compounds, such as phosphorus-containing compounds, are analyzed according to frequency.

T_1: "Spin-lattice" relaxation time. A time constant that reflects the rate at which excited protons exchange energy with the surrounding environment.

T_2: "Spin-spin" relaxation time. A time constant that reflects the rate at which protons stop rotating in phase with each other because of the local magnetic fields of adjacent nuclei.

Tesla: A unit of measurement of the magnetic force per unit area that can be generated within a defined region; 1 tesla = 10,000 gauss (10 kilogauss). For perspective, the magnetic field strength of the Earth is approximately half a gauss.

Tomographic scan: The image of an individual slice or plane.

Glossary of Acronyms

ACR — American College of Radiology
AMI — American Medical International
ATP — adenosine triphosphate
BC/BS — Blue Cross and Blue Shield Association
CON — certificate of need
CT — computed tomography
DHHS — Department of Health and Human Services (United States)
DHSS — Department of Health and Social Security (United Kingdom)
DRG — diagnostic related group
ECG — electrocardiogram
EMI — English Music Industry
FDA — Food and Drug Administration, DHHS
FDCA — Food, Drug, and Cosmetic Act
FONAR — field focusing nuclear magnetic resonance
GE — General Electric Co. (United States)
GEC — General Electric Co. (United Kingdom)
HCA — Hospital Corporation of America
HCFA — Health Care Financing Administration, DHHS
HIAA — Health Insurance Association of America
HMO — health maintenance organization

HSA — Health Systems Agency
IDE — investigational device exemption
IGC — Intermagnetics General Corp.
IRB — Institutional Review Board
NCI — National Cancer Institute, NIH
NEMA — National Electrical Manufacturers Association
NHLBI — National Heart, Lung, and Blood Institute, NIH
NHPIC — National Health Planning Information Center
NIH — National Institutes of Health, DHHS
NME — National Medical Enterprises, Inc.
NMR — nuclear magnetic resonance
NRPB — National Radiological Protection Board (United Kingdom)
NSF — National Science Foundation
OHTA — Office of Health Technology Assessment, DHHS
PDP — Product Development Protocol
PET — positron emission tomography
PMA — premarket approval
PMAA — premarket approval application
PPO — Preferred Provider Organization
RCHSA — Radiation Control for Health and Safety Act
R&D — research and development
RF — radiofrequency waves
SBIR — Small Business Innovation Research program
SHCC — Statewide Health Coordinating Council
SHPDA — State Health Planning and Development Agency
SPECT — single photon emission computed tomography
SUNY — State University of New York
UCR — usual, customary, and reasonable charges
UCSF — University of California, San Francisco
VA — Veterans Administration
YAG — yttrium aluminum garnet laser

Appendix E.—Acknowledgments and Health Program Advisory Committee

The authors are grateful to Mark Farfel at the Johns Hopkins School of Hygiene and Public Health for his contributions as a research assistant and are indebted to Charlotte Chalmers, Connie Pollack, and Amy Bohn for their expert assistance in manuscript preparation.

In addition, we wish to thank the many physician experts, scientists, hospital administrators, government officials, health planners, industry trade association officials and company representatives for the help and information they provided to us.

The following people, in addition to the advisory panel, provided valuable guidance.

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U.S. GOVERNMENT PRINTING OFFICE : 1984 O - 25-341 : QL 3

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OTA-HCS-27

SEPTEMBER 1984